ASTCT®
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August 29, 2026

Coverage and Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244-1850
Submitted electronically via CMS.gov and via CAGInquiries@cms.hhs.gov

Dear CMS Coverage and Analysis Group members:

The American Society for Transplantation and Cellular Therapy (ASTCT) is a professional membership association of more than 3,900 physicians, investigators, and other health care professionals. Our mission is to advance hematopoietic cell transplantation and cellular therapies through groundbreaking research, high-quality education, impactful advocacy, and clinical excellence.

ASTCT thanks CMS for the opportunity to provide comments on the Proposed Decision Memo associated with CAG-00444R2, Autologous Stem Cell Transplantation (AuSCT) for Multiple Myeloma. Our members are grateful that CMS has opened this issue for discussion, with the goal of broadening access to Medicare beneficiaries in need of SCT. ASTCT has successfully collaborated with the Coverage and Analysis Group at CMS on multiple occasions to improve coverage of SCT for Medicare beneficiaries and we have always appreciated the agency's detailed review of our comments and suggestions.

We are ready to assemble a group of myeloma SCT specialists and discuss any aspect of our comments further with your staff.

Regards,

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ASTCT President
2026-2027

Please send any correspondence to ASTCT Director of Government Relations, Molly Ford, at MFord@astct.org.

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Request Summary

ASTCT appreciates the opportunity to provide comments to the Centers for Medicare & Medicaid Services (CMS) regarding the proposed decision memorandum for CAG-00444R2, focused on changes to NCD 110.23 – Stem Cell Transplantation. ASTCT fully supports modification of the current eligibility criteria in the NCD, as it is too restrictive to support the access to autologous stem cell transplant (AuSCT) that Medicare beneficiaries with multiple myeloma (MM) need. However, the membership of ASTCT feels the proposed changes continue to be too limiting and will leave a significant group of beneficiaries who can benefit from AuSCT without that treatment option.

The revised NCD language CMS is proposing reads as follows:

> Effective October 1, 2000, single AuSCT is ~~only~~ covered for Stage II or III patients using Durie Salmon or International Staging System and its revisions that fit the following requirements.
> - Newly diagnosed or responsive multiple myeloma. This includes those patients with previously untreated disease, those with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein [serum and/or urine] or in bone marrow infiltration, sustained for at least 1 month), and those in responsive relapse; and
> - Adequate cardiac, renal, pulmonary, and hepatic function.

ASTCT proposes the the following changes to the coverage language, with proposed alternate text in green:

> Effective [Date, 2026], single AuSCT is **covered for Multiple Myeloma patients with active disease, as defined by International Myeloma Working Group diagnostic criteria.**
> - ~~Newly diagnosed or responsive multiple myeloma. This includes those patients with previously untreated disease, those with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein [serum and/or urine] or in bone marrow infiltration, sustained for at least 1 month), and those in responsive relapse; and~~
> - ~~Adequate cardiac, renal, pulmonary, and hepatic function.~~

If CMS decides to retain a staging-based system, ASTCT requests the language read as follows:

> Effective [Date, 2026], single AuSCT is ~~only~~ covered for ~~Stage II or III~~ **any stage** patients using Durie Salmon or International Staging System and its revisions.

- ~~Newly diagnosed or responsive multiple myeloma. This includes those patients with previously untreated disease, those with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein [serum and/or urine] or in bone marrow infiltration, sustained for at least 1 month), and those in responsive relapse; and~~
- ~~Adequate cardiac, renal, pulmonary, and hepatic function.~~

ASTCT has identified a substantial body of evidence to support the key tenets of our request, as outlined in the below sections. Given the limitations of the comment portal, we are separately sending an email to CAGInquiries@CMS.gov with the full list of references and their main points.

AuSCT is a broadly safe and effective treatment option

ASTCT first wants to remind CMS and other stakeholders that AuSCT is a well-established, safe and effective treatment option that is extremely well-tolerated by most transplant candidates. The Center for International Blood and Marrow Transplant Research has collected data on more than 188,000 patients receiving AuSCT since 2002 and reports that the 3-year probability of survival for patients receiving their first AuSCT between 2019-2023 is 83.9%, with a 95% confidence interval of 83.5%-84.2%. When looking at multiple myeloma patients specifically, the survival probability is higher – to 86.9%, based on more 38,000 patients receiving AuSCT during the 2019-2023 timeframe. [1] While AuSCT has always been relatively low-risk, its safety profile has improved significantly – specifically, an increase of 15% in 3-year survival - since the time CMS was making its initial determination as to which beneficiaries with MM would be eligible for AuSCT. We encourage CMS to keep these improvements in patient safety and survival in mind when considering the issue of patient eligibility.

Eligibility for SCT should be based on active disease status

ASTCT appreciates the efforts CMS has initiated to modernize the disease staging criteria within the NCD. However, the use of any staging system is no longer the most accurate way to determine which patients require therapy. Instead, patients are evaluated based on their diagnostic criteria and – more precisely - whether they have smoldering (pre-cancerous) or active (cancerous) disease. Once an individual has active disease, there is no returning to an asymptomatic or smoldering state and patients need to have all treatment options available to them, including AuSCT. The NCCN guidelines for symptomatic (active) MM support this perspective and are clear in their recommendations for primary treatment – initiate myeloma therapy to limit systemic damage and assess for candidacy for AuSCT.[2]

[1] Broglie L, Xu K, Oloyede T, Chen M, Allbee-Johnson M. Current Uses and Outcomes of Cellular Therapy in the US, Summary Slides 2025. https://cibmtr.org/CIBMTR/Resources/Summary-Slides-Reports#USsummarySlides
[2] National Comprehensive Cancer Network. Multiple Myeloma Guidelines, Version 5.2026 – January 9, 2026. https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf

CMS' initial use of Durie-Salmon stages II and III was logical for the time in which it was referenced during the expansion of the NCD to include MM in August 2000, as Durie-Salmon stage I included a mix of patients with active (cancerous) disease as well as smoldering (pre-cancerous) patients without clear tools to understand and separate those groups. The International Staging System was introduced in 2005 to replace Durie-Salmon, with the goal of using a duo of easily accessible blood tests to classify patients into three prognostic groups or stages and it has grown and changed from that point. While the ISS remains a significant improvement from Durie-Salmon and ASTCT appreciates CMS' acknowledgement of future iterations with the agency's use of "the ISS and its revisions," the use of any staging system will require ongoing monitoring and NCD maintenance from CMS as nomenclature changes with clinical practice in the future.

Alternatively, modifying the coverage language to focus on active disease will allow for the most benefit to Medicare patients with MM while simultaneously requiring the least future revision to the NCD. Active MM is defined by the International Myeloma Working Group [IMWG], a scientific advisory board tied to the International Myeloma Foundation whose mission is "*to conduct collaborative basic, clinical, and translational research to improve outcomes for myeloma patients while providing scientifically validated, critically appraised consensus guidelines for the myeloma community globally*."[3]

The IMWG refines and updates its definition for active multiple myeloma as needed based on the accumulation of additional evidence in the scientific literature. The current definition of active multiple myeloma is a greater than 10% amount of clonal bone marrow plasma or biopsy-provden bony or extramedullary plasmacytoma and any one or more of the CRAB criteria and myeloma-defining events, including biomarker levels, lesions and cell counts.[4] As demonstrated by the detailed criteria in this definition, the IMWG's standards are both specific and clinically relevant. The IMWG is recognized as the authoritative source on diagnostic criteria for multiple myeloma and could be utilized by CMS as the main resource for defining active multiple myeloma in the final NCD language.

Evidence supports the use of AuSCT in patients with ISS Stage I disease

As stated in the prior section, limiting coverage for AuSCT to MM patients with stage II and III excludes individuals that can and do benefit significantly from this treatment option. While ASTCT still believes that a focus on active disease should be the primary eligibility criterion for Medicare coverage, we ask that any staging-based system be inclusive of stage I – or utilize an

[3] International Myeloma Foundation. International Myeloma Working Group. Accessed August 23, 2026. https://www.myeloma.org/international-myeloma-working-group

[4] International Myeloma Foundation. IMWG criteria for the diagnosis of multiple myeloma. Accessed August 26, 2026. https://www.myeloma.org/international-myeloma-working-group-imwg-criteria-diagnosis-multiple-myeloma

"any stage" phrasing – to allow for the treatment of individuals that are stage I and should be treated with AuSCT.

The primary Phase II and III reference trials for AuSCT in MM have all included patients of any stage – and have demonstrated a favorable response across stages. In the DETERMINATION trial, the median progression-free survival (PFS) was 67.5 months with induction therapy plus AuSCT versus only 46.2 months with induction therapy alone. In the ISS I subgroup, median PFS was not reached with AuSCT versus 52.0 months without AuSCT and the reported hazard ratio (HR) was 1.83 [95% confidence interval (CI), 1.32–2.54), favoring AuSCT.[5] The IFM 2009 trial of AuSCT, conducted in France, reached similar conclusions. Median PFS was 50 months with AuSCT versus 36 months overall. ISS did not modify the treatment effect (interaction P=0.98), and investigators reported benefit across ISS strata.[6]

Because all patients with active MM benefit from AuSCT, no society guidelines (including ASCO, NCCN, and IMWG) use staging of any type as a tool to triage AuSCT access. The same is the case across the landscape of virtually all healthcare payers, including commercial US insurers. Similarly, NICE guidelines from the United Kingdom – which also factor cost-effectiveness into account – similarly do not use staging to dictate coverage for AuSCT.[7]

CMS should not define transplant candidacy beyond diagnosis in the NCD

Separate from the drafted modifications to the staging systems discussed in the proposed decision memo, CMS retains the following qualifications:

- "Newly diagnosed or responsive multiple myeloma. This includes those patients with previously untreated disease, those with at least a partial response to prior chemotherapy (defined as a 50% decrease either in measurable paraprotein [serum and/or urine] or in bone marrow infiltration, sustained for at least 1 month), and those in responsive relapse; and
- Adequate cardiac, renal, pulmonary, and hepatic function."[8]

ASTCT appreciates CMS' intention that AuSCT should only be provided to beneficiaries for whom the procedure would be considered predictably safe. However, in direct parallel with the aging of the references to staging systems, the specificity of this language is no longer aligned with how transplant specialists evaluate patient candidacy for AuSCT.

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[5] Richardson PG, Jacobus SJ, Weller EA, et al. Triplet therapy, transplantation, and maintenance until progression in myeloma. N Engl J Med. 2022;387:132-147. Supplementary Appendix, Figures S3-S4.

[6] Attal M, Lauwers-Cances V, Hulin C, et al. Lenalidomide, bortezomib, and dexamethasone with transplantation for myeloma. N Engl J Med. 2017;376:1311-1320.

[7] United Kingdom National Institute for Health and Care Excellence (NICE). Myeloma: diagnosis and management guideline. NG35, Published February 10, 2016; Updated October 25, 2018. https://www.nice.org.uk/guidance/ng35/chapter/Recommendations

[8] CMS.gov. National Coverage Analysis Proposed Decision Memo: Autologous Stem Cell Transplantation (AuSCT) for Multiple Myeloma. Accessed August 23, 2026. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=366

ASTCT notes that CMS refrains from adding this level of specificity to most other indications in the NCD, appropriately leaving the determination of individual candidacy for treatment to the clinical experts. When evaluating an individual patient for whether AuSCT is an option, the transplant clinical teams take physiologic fitness, comorbidities, organ function, disease characteristics, and informed patient preference into account. These factors – which are far beyond what the current NCD specifies - are considered to be core clinical practice benchmarks. ASTCT has an on-going and robust workstream devoted to the review and updating of practice guidelines, which includes evidence-based reviews, clinical comparator tools and disease-specific[9] position statements, including guidelines focused on geriatric patients.[10] These resources are publicly available to support individual clinicians in their decision-making processes and are updated regularly to integrate the most recent research and evidence refinement.

ASTCT requests that CMS remove the current language about transplant candidacy and allow clinicians, supported by a robust body of literature and guidelines, to assess stem cell transplant as a treatment option on an individual beneficiary basis.

CMS could issue a revised proposed decision memo to seek additional input

ASTCT appreciates CMS' efforts to reduce the timeline associated with changes to an NCD by issuing a proposed decision memo immediately, rather than flow through the full-length National Coverage Analysis process. However, this modification did not allow an opportunity for ASTCT and other stakeholders outside of the original requester group to share thoughts that may have shaped a different proposed decision. Given the current proposed decision memo, the majority of comments will likely focus on asking CMS to expand the proposed language to include Stage I patients. However, ASTCT feels strongly that our proposal to focus on disease status instead of staging would be both more durable language for CMS to utilize in an NCD and would be the preferred option for clinicians if the opportunity for more robust discussion of modifications would have been presented. ASTCT encourages CMS to consider a second proposed decision with another 30-day comment period to allow for additional dialogue and discussion with the patient and clinical treatment communities.

[9] American Society for Transplantation and Cellular Therapy. ASTCT Clinical Practice Recommendations for Transplantation and Cellular Therapies in Multiple Myeloma. June 2022. Accessed August 26, 2026. https://www.astctjournal.org/article/S2666-6367(22)01166-6/fulltext
[10] American Society for Transplantation and Cellular Therapy. Practice Guidelines. Accessed August 23, 2026. https://www.astct.org/Education/Practice-Guidelines

Contact Information

ASTCT welcomes the opportunity to meet with CMS to discuss any of the issues raised in this letter in greater detail and would be pleased to engage on any technical questions the agency may have. Please contact Molly Ford, ASTCT's Director of Government and Payer Relations, at mford@astct.org, with any questions or to arrange a meeting.

Appendix: Literature Summary

The evidence supports treating ISS as a prognostic measure, not a transplant-eligibility exclusion. It also supports evaluating older adults according to physiologic fitness, comorbidity, organ function, disease biology, and informed patient preference.

Hazard-ratio interpretation note: The trials use different reference groups. In IFM 2009, EMN02/HO95, and FORTE, an HR below 1 favors AuSCT. In DETERMINATION, the comparison is reversed. It compares RVd alone with RVd plus AuSCT, so an HR above 1 favors AuSCT. The stated treatment comparison must therefore be considered when interpreting each HR.

Coverage question	Evidence summary	Evidence strength and coverage relevance
Benefit across ISS stages I–III	Four randomized studies consistently demonstrate improved progression-free survival (PFS) or depth of disease control with upfront AuSCT. [1–4] **DETERMINATION:** Overall median PFS was 67.5 months with RVd plus AuSCT versus 46.2 months with RVd alone. In the ISS I subgroup, median PFS was not reached with AuSCT versus 52.0 months without AuSCT. The reported HR was 1.83 (95% CI, 1.32–2.54), favoring AuSCT. Estimates also numerically favored AuSCT in ISS II (HR 1.38; 95% CI, 0.96–1.96) and ISS III (HR 1.14; 95% CI, 0.64–2.01).[3] **IFM 2009:** Median PFS was 50 versus 36 months overall (HR 0.65). ISS did not modify the treatment effect (interaction P=.98), and investigators reported benefit across ISS strata.[1] **EMN02/HO95:** Median PFS was 56.7 versus 41.9 months (HR 0.73). Benefit was	The evidence is strengthened by four randomized trials using different induction and maintenance strategies, all showing a consistent disease-control advantage with AuSCT. ISS was incorporated into trial eligibility, stratification, or subgroup analysis, and IFM 2009 found no evidence of treatment-effect heterogeneity by ISS stage. Stage-specific analyses were not designed as separate trials, so the smaller ISS II and III estimates are appropriately interpreted together with the overall randomized results and interaction analyses. Although overall-survival differences have not been consistently demonstrated, PFS and response depth are clinically meaningful outcomes in multiple myeloma. Collectively, the evidence supports access across ISS I–III and

	retained across prespecified prognostic groups, including patients with ISS II/III disease (HR 0.72; 95% CI, 0.59–0.87).[2] **FORTE:** In an exploratory comparison, 4-year PFS was 69% with KRd plus AUSCT versus 56% with KRd12 (HR 0.61; 95% CI, 0.43–0.88). Randomization was stratified by ISS I versus II/III.[4]	identifies no ISS stage that should be categorically excluded from AuSCT coverage.
Adults aged ≥65	Seven studies directly evaluate selected older adults, including patients aged ≥70, ≥74, and ≥75.[5–11] **Merz:** Safety, event-free survival, and overall survival did not differ significantly among transplanted patients aged 60–64, 65–69, and 70–75. ISS and cytogenetic risk were more prognostic than age.[5] **Rago:** Selected AuSCT recipients aged 70–74 had median PFS of 56.4 months and overall survival of 107.6 months.[6] **Joseph:** Among patients aged ≥74, there were no 100-day transplant-related deaths. Median PFS was 50 months and overall survival was 80 months in AuSCT recipients.[7] **Klein:** Age did not affect PFS or overall survival after first-line AuSCT, whereas comorbidity predicted the need for higher-level supportive care.[8] **CIBMTR 2020:** Among 2,092 recipients aged ≥70, age ≥70 was not associated with statistically significant differences in nonrelapse mortality, relapse, PFS, or overall survival compared with ages 60–69 under the prespecified significance threshold.[9] **CIBMTR 2021:** Among 360 recipients aged ≥75, 100-day mortality was 1%, 2-year PFS was 66%, and 2-year overall survival was 83%.[10] **Worldwide registry:** Among 61,797 recipients, 3-year overall survival was	This evidence is strengthened by its scale, consistency, and representation of real-world practice. It includes institutional cohorts, multicenter studies, CIBMTR analyses, and a worldwide registry of more than 61,000 recipients. The studies also evaluate clinically relevant thresholds beyond age 65, including ages 70, 74, and 75 or older. Because these are observational studies of selected recipients, they are most informative about feasibility, safety, and outcomes in patients considered suitable for transplantation. That is directly aligned with the proposed coverage standard, which calls for individualized selection rather than transplantation based on age alone. The findings support access to AuSCT evaluation for adults aged ≥65 without implying that every older adult is an appropriate candidate.

	81.1% at ages 65–69, 78.4% at 70–74, and 74.8% at ≥75. Adjusted excess mortality was similar across age groups.[11]	

In summary, the evidence supporting coverage is strengthened by:

- Consistent improvement in PFS or depth of disease control across four randomized trials.
- Representation of all ISS stages, including direct evidence of substantial benefit in ISS I and no evidence that ISS stage should determine AuSCT exclusion.
- Favorable safety and survival outcomes in appropriately selected adults aged ≥65, including patients aged ≥70 and ≥75.
- Consistent findings across institutional, multicenter, national registry, and worldwide registry studies.

The evidence therefore supports access to frontline AuSCT across ISS stages I–III and for appropriately selected adults aged ≥65 without a fixed upper-age cutoff. Eligibility should be determined through an individualized assessment of physiologic reserve, functional status, frailty, comorbidity, organ function, disease biology, anticipated benefits and toxicity, alternative treatments, and patient goals.

This coverage approach would enable medically appropriate transplant evaluation. It would not require or presume that AuSCT is appropriate for every patient. The ultimate treatment decision should remain individualized and made through shared decision-making between the patient and treating transplant team.

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