

MSAC Application 1832

**Detection of measurable residual
disease (MRD) in patients with multiple
myeloma (MM)**

PICO Set

Population

Describe the population in which the proposed health technology is intended to be used:

The proposed health technology is intended to be used in patients with multiple myeloma (MM) requiring assessment of measurable residual disease (MRD) to determine treatment response and monitor for the risk of relapse. MRD testing is proposed at key treatment milestones: such as during therapy when a patient achieves a complete response to treatment to confirm the depth of response and inform subsequent clinical management and during the maintenance phase of treatment, where MRD-status is used to monitor the risk of relapse and inform risk-adapted treatment strategy.

MM is a rare, progressive, malignant disorder of the plasma cells (Padala et al. 2021). In Australia, over 2,700 people are diagnosed with MM annually, comprising 1.6% of all new cancer cases diagnosed. The average 5-year survival rate in Australia is 61%, being 59.8% for males and 61.8% for females (Cancer Australia 2025). There are over 1,200 deaths attributed to MM in Australia annually, representing 2.3% of all deaths from cancer.

MM is a relapsing-remitting cancer, meaning people will experience periods of disease control (remission), followed by periods when the disease is active (relapse). Relapse is a nearly inevitable consequence of MM, with 10% of patients with MM experiencing an early relapse within one year of initiating treatment (Yan et al. 2024). Patients experience worsening duration of treatment response, median survival and quality of life at each successive line of treatment (Chim et al. 2018; Rodríguez-Lobato et al. 2025) underscoring the importance of achieving a deep and long-lasting remission at the first-line of treatment.

Initial treatment for newly diagnosed MM depends on their eligibility for high dose therapy and autologous stem cell transplant (ASCT) which is determined based on the patient's age, comorbidities and functional status. ASCT offers patients with the best chance for achieving deep and long-lasting remission (MMRF 2026). Prior to ASCT, patients receive high-intensity induction therapy to reduce tumour burden and improve the duration of transplant (Myeloma Australia 2026a). Transplant-ineligible patients often experience worse outcomes compared to transplant-eligible patients due to advanced age, frailty, comorbidities and high discontinuation rates (Jung 2025). Wherever possible, patients should be considered for a clinical trial. Otherwise, transplant-ineligible patients are recommended to receive continuous daratumumab-based combination regimens until disease progression (Myeloma Australia 2026d). Other therapies for first-line transplant-ineligible MM include bortezomib, lenalidomide and dexamethasone (VRd) or bortezomib, cyclophosphamide and dexamethasone (VCD) (Myeloma Australia 2026d).

If a patient is refractory to treatment or relapses after an initial period of response, termed relapsed or refractory MM (RRMM), treatment options in subsequent lines are combinations incorporating lenalidomide, pomalidomide, bortezomib, carfilzomib and daratumumab, among others (Quach 2022). The most common 2L therapy currently is a combination consisting of daratumumab, bortezomib and dexamethasone (DVd)(Quach 2022).

Following the initial course of treatment, patients often receive maintenance therapy to prolong progression-free survival (PFS). Typically, this consists of lenalidomide as monotherapy, if the patient received lenalidomide-based induction therapy (Myeloma Australia 2026b). In patients who received DVd as a 2L treatment, maintenance therapy consists of daratumumab monotherapy after the initial 8 cycles (Facon et al. 2019).

Maintenance is usually continued indefinitely until disease progression or toxicity. However, this requires careful balancing of treatment benefits against toxicity and quality of life impacts (Myeloma Australia 2026b). Continued exposure to anti-myeloma treatments can have negative impacts on quality of life due to the accumulated toxicity and side effects from treatment which can include fatigue, gastrointestinal effects, and muscle cramping (Grossman and Crumrin 2026). Indefinite use of maintenance therapy also carries a risk in the development of secondary cancers (Kumar et al. 2026). During maintenance therapy, patients are monitored for relapse, which may necessitate the initiation of new therapy. Not all patients with relapsed MM require immediate treatment and may require a 'watch and wait' approach. However, patients presenting with clinical relapse should begin therapy without delay (Myeloma Australia 2026c).

MRD refers to the detection of small amounts of cancer cells that remain in the body during or after treatment, and MRD-status is being used more often as a surrogate endpoint for PFS and overall survival (OS) in clinical trials, reflecting its growing relevance to clinical practice (Sonneveld et al. 2024). MRD-negative status is strong prognostic factor for PFS and OS and growing evidence supports MRD testing to guide treatment decisions (Chen et al. 2026).

This application requests MBS funding for MRD testing for patients diagnosed with MM, where testing would be used to guide decision-making and inform clinical management. The proposed use of MRD testing is to confirm the depth of response such as when a patient achieves a complete response or better by traditional methods, at key treatment milestones, such as post-ASCT or during maintenance therapy, aligned with clinical expert consensus (Chen et al. 2026; Ramasamy et al. 2023). Confirmed MRD-negativity status with concurrent achievement of complete response may support the de-escalation or safe discontinuation of therapy, whereas discordant MRD-positivity may suggest persistent disease that may benefit from treatment intensification. This application also requests MRD testing to inform monitoring for relapse during maintenance therapy. MRD testing can detect disease resurgence before symptoms of clinical relapse emerge, enabling clinicians to adopt a risk-adapted treatment strategy (Chen et al. 2026).

Specify any characteristics of patients with, or suspected of having, the medical condition, who are proposed to be eligible for the proposed health technology, describing how a patient would be investigated, managed and referred within the Australian healthcare system in the lead up to being considered eligible for the technology:

This application requests MBS funding of MRD testing for MM patients as an adjunctive service to existing diagnostic and assessment tests. MRD testing is proposed at key treatment milestones, when a patient achieves a complete response to treatment, and for disease monitoring during maintenance or remission. MRD testing is intended to supplement current standard of care by providing a more sensitive assessment of depth of response to treatment and detecting early risk of relapse to better inform treatment decisions.

The population proposed in this application are adult patients diagnosed with MM who are currently receiving active anti-myeloma therapy, or who have discontinued therapy and require monitoring for potential disease recurrence.

Diagnosis is typically prompted by clinical suspicion in patients with active symptomatic MM, presenting with non-specific symptoms or warning signs such as unexplained anaemia, persistent bone pain, hypercalcaemia, renal impairment or recurrent infections (Pires et al. 2025). MGUS and SMM are managed through active monitoring, and treatment is only initiated once the condition progresses to MM.

Various blood-based, urine and bone marrow tests are used to detect abnormalities in biochemical parameters to establish a diagnosis of MM. Some of these tests may be ordered by the patient's GP, with referral to a haematologist for diagnosis if there is strong clinical suspicion or upon the receipt of abnormal findings. Only the haematologist can order a bone marrow biopsy for a definitive diagnosis (Cancer Council 2026). The current 2014 International Myeloma Working Group (IMWG) guidelines state that a diagnosis of active MM must include both i) the presence of monoclonal plasma cells in the bone marrow $\geq 10\%$ or biopsy-proven bony or extramedullary plasmacytoma and 2) evidence of at least one SLiM-CRAB myeloma-defining event presented in Table 1 (International Myeloma Foundation 2026; Pires et al. 2025).

Table 1 2014 IMWG guidelines for diagnosis of MM

Presence of monoclonal plasma cells in the bone marrow $\geq 10\%$ or biopsy-proven bony or extramedullary plasmacytoma
AND
Evidence of at least one SLiM-CRAB myeloma-defining event: S: myeloma-defining biomarkers of at least 60% clonal plasma cells present in the bone marrow Li: involved/uninvolved light chain ratio of 100 or more in the blood M: MRI findings of more than 1 focal lesion C: calcium elevation R: renal insufficiency A: anaemia B: bone lesions

Abbreviations: IMWG, International Myeloma Working Group; MM, multiple myeloma; MRI, magnetic resonance imaging;
Source: Pires et al. (2025), International Myeloma Foundation (2026)

A patient diagnosed with active symptomatic MM requires prompt treatment. This application proposes MRD testing in MM patients receiving treatment to assess the depth of treatment response and inform subsequent clinical management. MRD testing is proposed as an adjunctive service in addition to routine diagnostic services (blood-based, urine-based, bone marrow biopsy and advanced imaging) which are currently used to assess response to treatment.

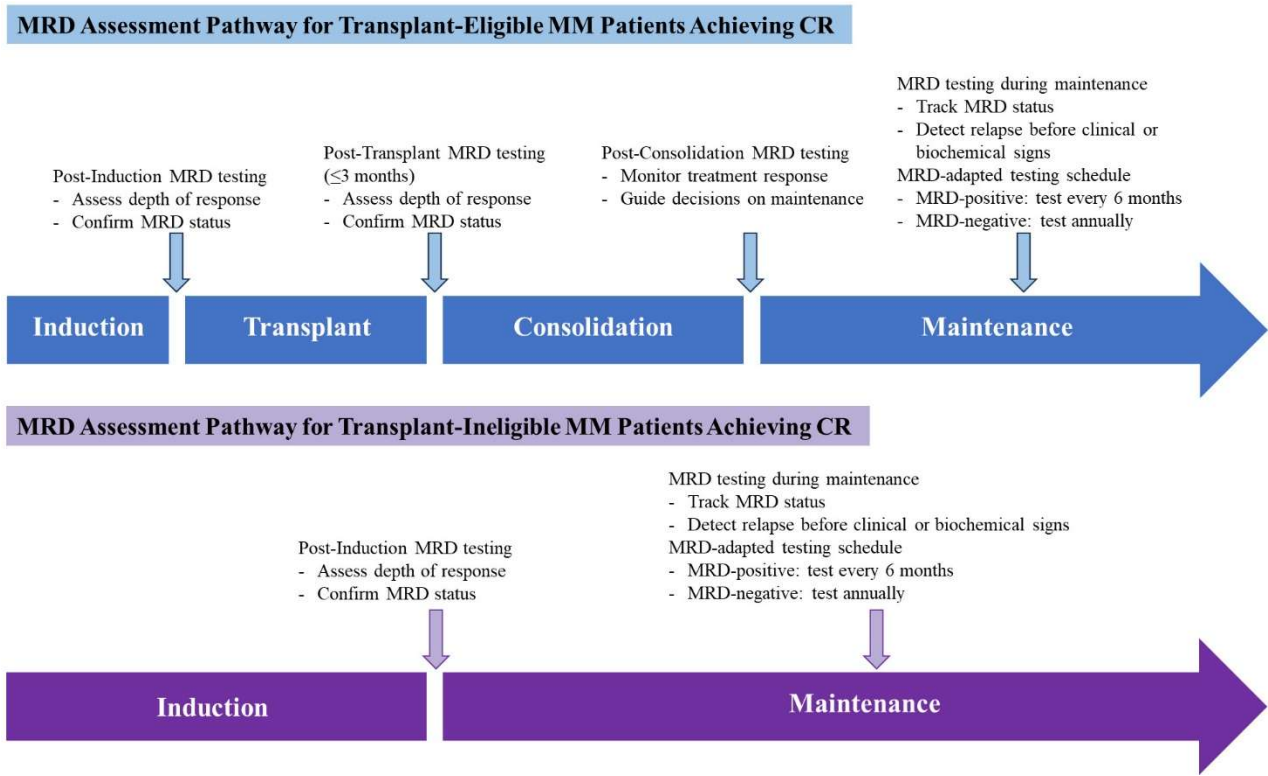
MRD is proposed to be used once a patient achieves a complete response according to routine assessment, to assess the depth of response. However, the timing and use of MRD testing may be determined at the clinician’s discretion, informed by individual patient circumstances and the potential clinical utility of the test results. Evidence shows that MRD negativity is an independent prognostic factor irrespective of CR (Paiva et al. 2022). In patients who would value the prognostic information, MRD could be considered. Given the invasiveness of a bone marrow biopsy required for testing, it is not expected that MRD testing will be used in the absence of clinical value. The Applicant is open to considering MRD testing when a patient achieves a very good partial response, subject to further input from clinicians and patients.

Test information results in the change in clinical management if MRD status is positive or otherwise supports the informed decision to de-escalate, proceed to maintenance or discontinue treatment safely. This application also requests MRD testing to inform monitoring for relapse during maintenance therapy or after treatment discontinuation. MRD testing can detect disease resurgence before symptoms of clinical relapse emerge, enabling clinicians to adopt a risk-adapted treatment strategy (Chen et al. 2026).

The timing and frequency of MRD testing is tailored to treatment phase as presented in Figure 1. In summary, patients receiving ASCT are indicted for MRD testing upon achieving a complete response at the following treatment phases: post-induction, post-transplant, post-

consolidation (if indicated), and for monitoring during maintenance therapy. In non-eligible ASCT patients, MRD is indicated if the patient achieves a complete response post-induction, and for monitoring during maintenance therapy.

Figure 1 Proposed use of MRD testing for assessing response to therapy in MM patients



Abbreviations: CR, complete response; MM, multiple myeloma; MRD, measurable residual disease
 Source: Chen et al. (2026)

Provide a rationale for the specifics of the eligible population:

MRD can detect residual disease in bone marrow at sensitivities up to 10⁻⁶ (FDA 2020) and as high as 10⁻⁷ (Derman et al. 2024), even in patients who have achieved a complete response based on blood and urine tests. However, MRD testing is unlikely to change clinical management for patients who have not achieved a complete response using traditional assessment methods. By contrast, for patients who have achieved a complete response, MRD testing may identify MRD-positivity and prompt a change in management. This application therefore requests MRD testing for MM patients receiving active treatment who have achieved a complete response by traditional methods, where results may inform subsequent treatment decisions. However, the timing and use of MRD testing may be determined at the clinician's discretion, informed by individual patient circumstances and the potential clinical utility of the test results. Evidence shows that MRD negativity is an independent prognostic factor irrespective of CR (Paiva et al. 2022). In patients who would value the prognostic information, MRD could be considered. Given the invasiveness of a bone marrow biopsy required for testing, it is not expected that MRD testing will be used in the absence of clinical value. The Applicant is open to considering MRD testing when a patient achieves a very good partial response, subject to further input from clinicians and patients.

MRD testing is also proposed for patients who have discontinued therapy, to monitor for risk of biochemical recurrence before clinical symptoms of relapse. This would enable earlier

identification of relapse and trigger appropriate monitoring to initiate therapy sooner and improve subsequent health outcomes.

Are there any prerequisite tests?

Yes. MRD testing will be conducted in people with a confirmed diagnosis of MM who are currently receiving active MM treatment, and achieve a complete response assessed via current assessment services. Traditional assessments of response assessment include serum and urine monoclonal protein (M-protein) testing, serum free light chains (sFLC), bone marrow biopsy to determine the proportion of clonal plasma cells and advanced imaging, such as positron emission tomography (PET) and magnetic resonance imaging (MRI).

As the test is proposed as an adjunctive service to existing monitoring, these tests will be done prior to MRD testing at each stage of response assessment.

Are the prerequisite tests MBS funded?

Yes

Provide details to fund the prerequisite tests:

Blood tests MBS items: 71200, 73370, 73391, 65060

Urine tests MBS items: 71057, 71059

Bone marrow biopsy MBS item: 30081, 30087

Imaging (X-rays, PET, MRI) MBS items: 61612, 61614, 63301, 58306

Intervention

Name of the proposed health technology:

MRD testing in MM with two brand-agnostic MBS items requested for different methodologies: multiparametric flow cytometry (MFC) or next-generation sequencing (NGS) assays.

Describe the key components and clinical steps involved in delivering the proposed health technology:

MRD testing is a highly sensitive technique used to detect small amounts of myeloma cells that may persist despite an assessment of complete response (Zabaleta et al. 2025) using the IMWG biochemical response classification (Gerlach 2025). Unlike current detection methods, MRD assessment allows for the discrimination between patients who appear to be in remission but harbor residual disease and those who achieve deep responses with minimal or no detectable tumour burden (Ho and Kourelis 2022; Meseha et al. 2024). Its high sensitivity also makes MRD a useful tool for monitoring disease and detecting signs of relapse.

Testing is performed in accredited pathology laboratories using bone marrow aspirate collected by during a bone marrow biopsy in outpatient or inpatient haematology settings. To minimise sampling bias, the first pull of aspirate should be used and handled according to an optimised bone marrow sampling protocol (Wijnands et al. 2023). The procedure can be performed both as an inpatient and as an outpatient service (PeterMac 2026). Patients are kept under observation following the procedure, and usually discharged on the same day, typically within 1-2 hours of the procedure (PeterMac 2026).

Assessment of MRD can be performed using flow cytometry or molecular sequencing. Although the submission requests assay-agnostic MBS items by methodology, the steps provided for NGS are specific to clonoSEQ by Adaptive Biotechnologies.

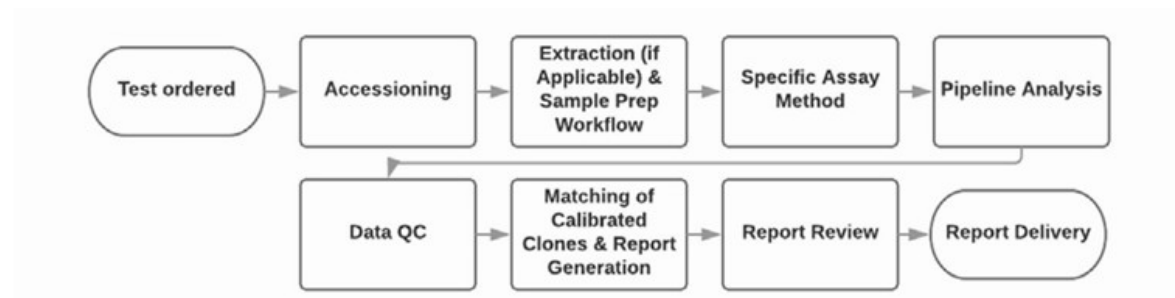
Next-generation sequencing

The clonoSEQ assay combines multiplex polymerase chain reaction with next-generation sequencing to identify and quantify the DNA sequences associated with MM. Specifically, the assay identifies IgH (VDJ), IgH (DJ), IgK and IgL receptor gene sequences, as well as translocated BCL1/IgH (J) and BCL2/IgH (J) for multiple myeloma (FDA 2020).

The steps consist of the following steps with the workflow presented in Figure 2 (FDA 2020):

1. Sample preparation: The assay requires a minimum genomic DNA (gDNA) input of 550 ng. 1 mL of bone marrow aspirate is requested to obtain sufficient extracted gDNA. The extraction method consists of lysing cells and denaturing proteins, after which DNA is bound to a substrate. Once the DNA is bound, a series of wash steps removes impurities. The DNA is eluted from the substrate. The extracted DNA is quantified using a spectrophotometer to measure the DNA concentration, of which a target of 20 µg of amplifiable gDNA is added to the assay. The MRD test can be performed with 500 ng – 20 µg of gDNA.
2. Library preparation: gDNA is amplified using locus-specific multiplex polymerase chain reaction (PCR) using V, D and J gene primers containing molecular barcodes to amplify IgH (VDJ), IgH (DJ), IgK, IgL BCL1/IgH (J), BCL2/IgH (J) and housekeeping gene (HKG) sequences. Internal controls in the PCR and sequencing steps are used to confirm that sufficient gDNA has been amplified and the amplification was successful. Reaction-specific index barcodes for sample identification are added to the amplified receptor sequences by PCR. Sequencing libraries are prepared by pooling barcoded amplified DNA. qPCR is used to verify the adequacy of the pooled amplified DNA library concentration.
3. Sequencing and data analysis: sequencing is conducted with the Illumina NextSeq™ 500 or 550 systems. The sequencing output is then processed by the bioinformatics pipeline software which conducts multiple quality control checks to confirm sequence accuracy, adequate DNA input, sufficient coverage and the absence of contamination. Sequencing reads are assessed for biological relevance, and dominant clonal sequences are evaluated for suitability as identifiers for disease tracking based on their abundance, uniqueness and detectability. In subsequent samples, these tracked sequences are compared against previously identified clones to determine whether MRD is present and whether it can be detected or quantified within the assay's validated sensitivity limits.
4. Issue of report: A Clonality (ID) report indicates the presence of dominant sequences residing within a presumed malignant lymphocyte clonal population, as identified in the baseline (diagnostic or high disease burden) sample from a patient. After one or more dominant sequence(s) have been identified in a baseline sample, subsequent samples from the same patient can be assessed for MRD after which a tracking report is generated. The MRD is expressed as a frequency that quantifies the level of residual disease based on the number of remaining copies of the initially dominant sequence(s) relative to the total number of nucleated cells in the sample.

Figure 2 clonoSEQ assay workflow



Abbreviations: QC, quality control
Source: FDA (2020)

Steps involved in flow cytometry

MFC is a laser-based laboratory test that relies on optical detection to identify and quantify cells or proteins. A single-cell suspension is stained with fluorophore-labelled antibodies for specific cellular markers targets (Biocompare 2023). The cells are then introduced into a flow cytometer, where a fluidics system directs them in a single file past an interrogation point. When a cell crosses an interrogation point, laser light is scattered and any bound fluorophores emit a fluorescent signal (Biocompare 2023). The fluorescence emitted is detected, amplified and converted into an electrical signal which can be analysed to identify distinct cellular populations (Biocompare 2023). MFC is highly susceptible to inter-rater and inter-laboratory variability due to the lack of standardised processes and the high degree of manual analysis involved (Robinson et al. 2026). Conventional analysis consists of drawing a region around a population of cells (known as gating) and applying that region to other parameters in the experiment, allowing the specific group of cells to be selected for further analysis for other markers (McKinnon 2018). Gating filters raw data to identify the cell population of interest for analysis and involves the exclusion of unwanted events from debris or dead cells. It is susceptible to operator bias and one of the biggest sources of variation in FC (Brinkman 2020).

One of the issues with MFC is the lack of standardisation due to the variability in instrument hardware which can emit and detect different fluorescent signals, differences in reagent and staining variation, and subjective data analysis (from gating) (Bio-Rad Laboratories Inc 2026).

Next-generation flow cytometry (NGF) builds on MFC. The term is used to capture the evolution of, and describe a modern approach to flow cytometry, but is often associated with the standardised protocol and platform by EuroFlow (Flores-Montero et al. 2017). The EuroFlow platform consists of protocols to standardise every step of the procedure and a validated fixed antibody panel utilising two-eight colour combinations rather than relying on user-defined targets to improve specificity and reliability (van Dongen et al. 2012)(Kumar et al. 2016). The platform also uses a bulk-lysis procedure to remove red blood cells from the bone marrow aspirate, and any debris and dead cells, concentrating the cell sample and enabling a higher limit of detection for improved sensitivity compared to traditional FC (Flores-Montero et al. 2017). NGF also utilises a semi-automated workflow with software assisted gating. A global reference database enables rapid sample comparison to reference samples during gating, resulting in a more reproducible analysis of results (Flores-Montero et al. 2017). Machine learning and mathematical algorithms result in the rapid identification of cells (Zhou et al. 2026). Although NGF aims to make gating reproducible, standardised and less operator dependent, certain elements of subjectivity are still introduced, especially when expert review is involved in the analysis (Szalat 2026).

Although NGF is a more sensitive, standardised application of flow cytometry, MPF is the broader and more accurate term for the procedure because it encompasses all flow cytometric assays that simultaneously assess multiple cellular markers, regardless of the platform, panel design, or level of standardisation. As advised by clinician input, the term is also more appropriate in many settings because access to NGF remains variable across institutions due to differences in instrumentation, standardisation requirements, expertise, and resource availability. Therefore, this submission requests MRD testing via MPF. To align with the IMWG criteria for MRD response, this application proposes a prerequisite sensitivity of 10^{-5} for flow cytometry methods, as presented in the proposed item descriptor.

Next-generation sequencing vs flow cytometry

The clonoSEQ Assay measures MRD to monitor changes in burden of disease during and after treatment to inform clinical decision-making and in conjunction with other clinicopathological features. The assay has built-in quality control mechanisms that enables real time differentiation between true biological absence of signal and failure due to poor DNA quality (Ching et al. 2020). This provides sample flexibility allowing the use of frozen, formalin fixed paraffin-embedded (FFPE) tissues or bone marrow smears (Szalat 2026), which may be partially degraded.

In comparison to flow cytometry, including NGF, NGS is more automated and less operator dependent, providing greater reliability and reproducibility of results (Szalat 2026). Importantly, molecular methods such as NGS offer a more precise measure of residual disease through higher sensitivity, detecting disease at sensitivities as low as 10^{-7} (Szalat 2026) potentially detecting MRD in patients who would otherwise be missed by flow cytometry, (Wang et al. 2022).

Because NGS identifies and quantifies MM-associated DNA sequences, it can identify a patient's specific clonotypes and track changes in disease-associated DNA over time. As a result, NGS requires a baseline pre-treatment sample to enable MRD assessment throughout the patient's disease course.

MPF is associated with a faster turnaround time, with less complex data analysis, but is restricted to the use of fresh samples. The samples must be analysed within a short time period of sample collection to avoid cell death, creating access and geographical limitations. Physicians should therefore choose the most appropriate methodology according to sample availability and resources. A comparison between NGS and MFC is presented in Table 2.

Table 2 Comparison between MFC and NGS

Characteristic	Multiparametric flow cytometry	Next-generation sequencing
Requires baseline sample	No	Yes, in order to identify clonotype and track
Sensitivity	$<10^{-5}$ *	$<10^{-6}$
Sample requirements	>5 million cells (more cells required to increase sensitivity to 10^{-6})	<2 million cells
Sample processing	Requires a fresh sample	Fresh or frozen sample
Assessment for haemodilution	Yes	Not possible
Turnaround time	2-4 days	7 days
Commercial availability	Reference or experienced in-house laboratory	clonoSEQ (Adaptive Biotechnologies)

Note: * NGS can reliably detect in 10^{-5} , but sensitivity of up to 2×10^{-6} has been reported under optimal conditions (Cassano et al. 2026; Urushihara et al. 2023)

Abbreviation: MFC, multiparametric flow cytometry; NGS, next-generation sequencing

Source: Adapted from Kumar et al. (2016); Yee and Raje (2021)

Identify how the proposed technology achieves the intended patient outcomes:

Many patients still relapse despite current assessments (serum and urine M-testing, sFLC, bone marrow biopsy and advanced imaging) indicating a deep response, reflecting a persistent disease that cannot be detected with the current assessment techniques (Kumar et al. 2016). MRD analysis detects residual myeloma cells at a sensitivity of 10^{-5} or greater, providing a more precise measure of depth of response. Acknowledging this, the IMWG have updated the response criteria to add a more detailed evaluation for deep response to include MRD assessment (Kumar et al. 2016). MRD assessments can be combined with current assessments and imaging techniques to detect extramedullary disease and depth of response (Wijnands et al. 2023). The outcome of MRD testing is dichotomous, with either a negative or positive test result determined at a defined sensitivity threshold. The IMWG criterion for MRD-negativity is defined at a minimum sensitivity of 10^{-5} or higher, which means fewer than 1 myeloma cell detected in a sample of 100,000 cells (Kumar et al. 2016).

MRD-negativity is a strong prognostic indicator for PFS and OS and can serve as a clinical endpoint to guide treatment goals. This has been demonstrated in multiple clinical studies where MRD assessments were taken (FORTE, CASSIOPEIA, PERSEUS, PATHEMA) and in meta-analyses (Munshi et al. 2020). Compared with MRD-positive disease, MRD-negative status showed improved PFS (hazard ratio [HR] of 0.33 [95% CI: 0.29, 0.37]) and OS (HR: 0.45 [95% CI: 0.39, 0.51]) across multiple patient populations, including in relapsed disease and high-risk disease (Munshi et al. 2020). The depth of MRD-negativity is also important, with patients who were able to achieve MRD-negative status at 10^{-6} by NGS, deeper than the recommended IMWG threshold of 10^{-5} , having superior outcomes in PFS and OS compared to those MRD-negative at 10^{-5} and 10^{-4} (Munshi et al. 2020). These observations are consistent across studies (Costa et al. 2023; Martinez-Lopez et al. 2024; Perrot et al. 2025; Perrot et al. 2018; Popat et al. 2024). Sustained MRD-negativity is similarly important, with patients in the POLLUX and CASTOR study who sustained MRD-negativity of over 12 months having the best PFS irrespective of treatment arm (Avet-Loiseau et al. 2021).

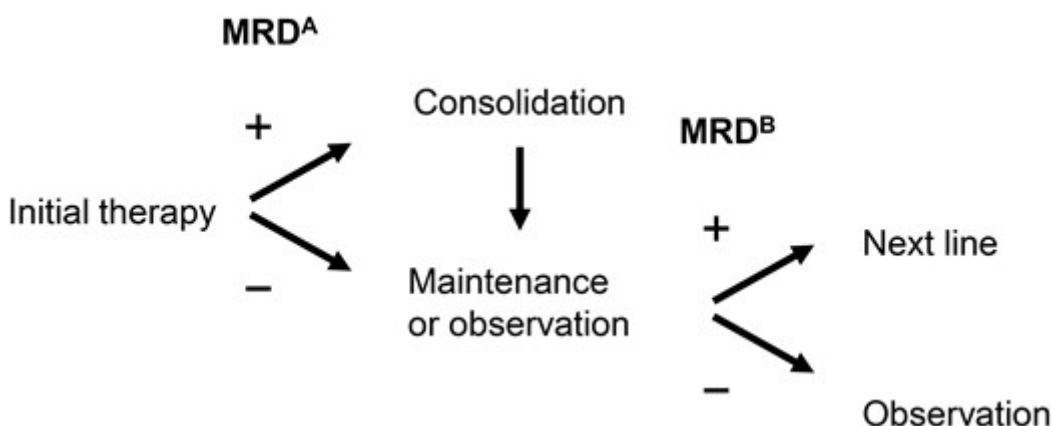
The management of MM consists of long-term treatment, either continuous therapy (doublet or triple regimen) until disease progression or maintenance treatment (typically monotherapy) following more intensive prior therapy such as ASCT. These treatments have been effective in prolonging PFS and OS but are highly toxic, and cumulative toxicity with prolonged exposure remains a concern (Dimopoulos et al. 2020; Martino et al. 2025).

MRD testing could help guide treatment by providing clinicians and patients with highly sensitive information to support decisions about safe treatment discontinuation, continuation, or intensification according to individual response, with the potential to improve outcomes and reduce costs. Sustained MRD-negativity following treatment can support the decision for safe treatment-de-escalation or cessation, if warranted (Chen et al. 2026; Ramasamy et al. 2023). Treatment de-escalation or maintenance cessation can reduce toxicities and provide cost-savings to the health system.

Confirmed MRD-positivity following treatment despite an achievement of complete response, triggers review and may prompt treatment intensification (Chen et al. 2026; Ramasamy et al. 2023). MRD assessment could then be re-assessed following subsequent treatment in a dynamic, risk-adapted approach.

Figure 3 provides an overview of how MRD would be utilised to guide treatment decisions.

Figure 3 MRD-guided treatment workflow for patients achieving complete response



Note: A, to guide treatment after initial therapy; B, to guide treatment on maintenance therapy
 Abbreviations: MRD, measurable residual disease; +, MRD-positive; -, MRD-negative
 Source: Yee and Raje (2021)

Emerging expert consensus supports a comprehensive approach that includes MRD assessment in treatment evaluation, combining bone marrow, imaging and peripheral blood-based assessment for a thorough assessment of depth of response (Chen et al. 2026; Ramasamy et al. 2023). The consensus is based on the growing evidence that achieving and sustaining MRD-negativity is strongly linked to improved outcomes.

A total of 94% of experts (n=17)(Chen et al. 2026) achieved consensus that MRD testing should be performed in all patients with MM and that MRD assessment should be incorporated into treatment evaluation.

A summary of key consensus recommendations are presented in Table 3. These recommendations inform the proposed frequency and timing of MRD testing in MM patients receiving active treatment in this application, as described in the population section.

Table 3 Summary of key consensus recommendations for the integration of MRD into MM management

Consensus statements	Agreement (n = 17)
The timing and frequency of MRD assessment are recommended to be tailored to the treatment phase. MRD testing is recommended for patients who achieve CR following a treatment course to confirm the depth of response. During maintenance therapy, MRD-positive patients should undergo MRD testing every 6 months, while MRD-negative patients should be tested every 12 months to monitor disease status.	94%
Dynamic MRD monitoring is recommended to track disease status over time and allow timely therapeutic decisions, such as early intervention for MRD resurgence and treatment intensification for persistent MRD.	100%
NGF and NGS are considered interchangeable for prognostic assessment of MRD-status in MM.	82%

Abbreviations: CR; complete response; MM, multiple myeloma; MRD, measurable residual disease; n, number of experts; NGF, next-generation flow cytometry; NGS, next-generation sequencing
 Source: Chen et al. (2026)

Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components?

No

Explain if it is essential to have this trademark component or whether there would be other components that would be suitable:

N/A

Are there any proposed limitations on the provision of the proposed health technology delivered to the patient (For example: accessibility, dosage, quantity, duration or frequency):

Yes, some limitations to the frequency or number of services delivered should be applied to ensure MRD testing is used to guide clinical management. Use of MRD testing is proposed to be tailored in frequency and timing according to treatment received and proposed to be used when a complete response to treatment is achieved. Because MRD testing requires a bone marrow aspirate, the invasiveness of the bone marrow biopsy procedure is expected to limit use to circumstances where results are likely to materially influence care, reducing the risk of overuse.

For disease monitoring, MRD monitoring is proposed annually (NCCN 2026) with the potential for more frequent monitoring of every 6 months for MRD-positive patients (Chen et al. 2026).

No specific restriction on frequency or number of services is presented in this application; however, it is anticipated that this will be refined through consultation with experts during the PICO development process.

Provide details and explain:

N/A

If applicable, advise which health professionals will be needed to provide the proposed health technology:

Specialist oncologist, haematologist or consultant physicians can order MRD testing, which is provided by approved pathologists in accredited laboratories.

If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:

N/A

If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:

Yes. The proposed services should only be referred by a specialist oncologist, haematologist or consultant physician.

Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?

Yes.

Provide details and explain:

The test would only be delivered in NATA accredited pathology laboratories by referral by registered medical practitioners (haematologists, oncologists and consultant physicians). The service should only be delivered by pathologists with NPAAC qualifications in genomic testing.

Indicate the proposed setting(s) in which the proposed health technology will be delivered:

(Select all relevant settings)

☐ Consulting rooms

- ☐ Day surgery centre
- ☐ Emergency Department
- ☐ Inpatient private hospital
- ☐ Inpatient public hospital
- ☒ Laboratory
- ☐ Outpatient clinic
- ☐ Patient's home
- ☐ Point of care testing
- ☐ Residential aged care facility
- ☐ Other (please specify)

All MRD assays (NGF and NGS) are performed in accredited pathology laboratories. Testing requires the use of bone marrow aspirate samples obtained from bone marrow biopsies. Bone marrow biopsies may occur during hospital admission or in outpatient settings, as required. In the outpatient setting, patients may attend day oncology or haematology units for sampling followed by a period of observation. Patients are usually discharged on the same day within 1-2 hours after the procedure.

Is the proposed health technology intended to be entirely rendered inside Australia?

Yes

Provide additional details on the proposed health technology to be rendered outside of Australia:

N/A

Comparator

Nominate the appropriate comparator(s) for the proposed medical service (i.e., how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian healthcare system). This includes identifying healthcare resources that are needed to be delivered at the same time as the comparator service:

Response to treatment is currently measured using the standard IMWG criteria, which includes assessment of serum and urine M-protein by electrophoresis, immunofixation or both, quantitation of plasma cells in bone marrow biopsy by immunohistochemistry, and sFLC assays (Kumar et al. 2016). Assessment of response measured via biochemical assessment is presented in Table 4. Additionally, biochemical response is often paired with functional imaging (PET or MRI), which checks for signs of metabolically active disease. Assessment of response measured via functional imaging is presented in Table 5.

The absence of metabolic lesions combined with an assessment of complete response measured by biochemical tests determines a deep response. In comparison, a discordant assessment between biochemical response and functional imaging suggests that the patient may not truly be in deep remission.

Table 4 Biochemical response classification (IMWG) - abridged

Category	Criteria
Complete response	Negative immunofixation on serum and urine M-protein; normalisation of FLC ratio; < 5% plasma cells in bone marrow

Partial response	≥ 50% reduction in M-protein; ≥ 90% reduction in urine M-protein or < 200 mg/24h; ≥ 50% reduction in plasma cells
Stable disease	Does not meet criteria for MR, PR, VGPR, CR or PD
Progressive disease	≥ 25% increase in M-protein, urine protein, or plasma cells; new lesions or clear progression of existing lesions

Abbreviation: CR, complete response; IMWG, International Myeloma Working Group; FLC, free light chains; h, hour; M-protein, monoclonal protein; mg, milligrams; MR, measurable response; PD, progression of disease; PR, partial response; VGPR, very good partial response

Source: Gerlach (2025)

Table 5 Functional imaging response classification (IMWG)

Category	Functional imaging criteria
Complete response	Deauville score < 4; reduced or absent uptake on PET; MRD
Partial response	Decreased lesion activity; stable or reduced standardised
Stable disease	No significant changes in uptake or activity
Progressive disease	New lesions; increased PET activity; significant MRI changes

Abbreviations: IMWG, International Myeloma Working Group; PET, positron emission tomography; MRD, measurable residual disease; MRI, magnetic resonance imaging

Source: Gerlach (2025)

A limitation of current methods for measuring treatment response is that the quantity of M-protein in the urine or serum may differ on a case-by-case basis. For example, a small proportion of cases may have non-secretory M-protein (Eslick and Talaulikar 2013), while assays differ in variability and subjectivity depending on laboratory practices (Dejoie et al. 2016). Traditional electrophoretic methods may not be sensitive enough to detect small changes in M-protein levels, especially in the early stages of disease which can cause false-negative results, leading to delays in detecting underlying disease and initiation of treatment (Binding Site 2026). Further, despite patients classified as achieving complete response by IMWG measures, most patients will experience relapse, reflecting persistent disease that cannot be detected using these methods (Kumar et al. 2016) and highlighting the limitations of current assessment methods.

MRD testing can detect trace amounts of myeloma cells that persist after treatment, including disease levels too low to identify microscopically, providing a more sensitive and reliable assessment of treatment response. When interpreted alongside existing assessments and complete response status, MRD testing supports more accurate response classification and can detect one cancerous cell per million healthy cells (sensitivity of 10^{-6}) with 20 µg of input DNA 95% of the time (Ching et al. 2020). Recent research has demonstrated that MRD-negative status surpasses the prognostic value of complete response achievement for PFS and OS (Lahuerta et al. 2017). Achievement of complete response in the absence of MRD-negativity was not associated with prolonged PFS and OS with near-complete response or partial response, whereas MRD-negativity was strongly associated with prolonged PFS and OS (Lahuerta et al. 2017). In combination, an achievement of complete response and MRD-negative status is the strongest prognostic factor for PFS and OS (Zabaleta et al. 2025), supporting the proposed use of MRD testing.

List any existing MBS item numbers that are relevant for the nominated comparators:

Blood tests MBS items: 71200, 73370, 73391, 65060

Urine tests MBS items: 71057, 71059

Bone marrow biopsy MBS item: 30081, 30087

Imaging (X-rays, PET, MRI) MBS items: 61612, 61614, 63301, 58306

Provide a rationale for why this is a comparator:

Current assessment of treatment response is multimodal. Multiple tests and services are used to determine treatment response and burden of disease. Not all tests and services may be ordered at the discretion of the physician.

Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator?

(Please select your response)

- ☒ None (used with the comparator)
- ☐ Displaced (comparator will likely be used following the proposed technology in some patients)
- ☐ Partial (in some cases, the proposed technology will replace the use of the comparator, but not all)
- ☐ Full (subjects who receive the proposed intervention will not receive the comparator)

Outline and explain the extent to which the current comparator is expected to be substituted:

MRD testing is proposed as an adjunctive service in addition to standard of care assessments of treatment response. MRD testing provides a measure of deeper response and should be used in combination with standard assessments according to the IMWG criteria for treatment response measured by biochemical tests and functional imaging (Table 4 and Table 5).

Outcomes

(Please copy the below questions and complete for each outcome)

List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

(Please select your response)

- ☒ Health benefits
- ☒ Health harms
- ☒ Resources
- ☒ Value of knowing

Outcome description – include information about whether a change in patient management, or prognosis, occurs as a result of the test information:

Health benefits

MRD testing is expected to provide prognostic value, informing the safe avoidance of continuing treatment or maintenance, and predictive value, predicting response to treatment including ASCT, and the risk of relapse during disease monitoring.

MRD testing is expected to result in a change in management (safe treatment de-escalation, or intensification) resulting in change in patient health outcomes (mortality, morbidity, quality of life).

Health harms

The MRD test itself is in-vitro, however the bone marrow biopsy procedure to obtain the sample for testing carries a risk of adverse events (such as haemorrhage, infection, pain). The procedure is relatively safe with a low rate of adverse events reported (<0.1%) (Bain 2005).

Health resources

MRD testing enables a risk-adapted approach to care, supporting treatment de-escalation or discontinuation in patients with sustained MRD negativity, optimising healthcare resource utilisation by providing cost-savings from treatment avoided.

Value of knowing

MRD testing provides clinicians and patients with reassurance and the confidence in treatment decisions. A study published by Chen and Tang (2014) highlights the importance of prognostic disclosure to patients, supporting the value of knowing from MRD testing. Australian survey data in haematological malignancies indicate that majority of patients expressing they wish to receive honest prognostic and life-expectancy information, with 87% expressing this preference (Button et al. 2022).

Proposed MBS items

How is the technology/service funded at present? (e.g., research funding; State-based funding; self-funded by patients; no funding or payments):

Some patients access MRD testing through clinical trials. Hospitals that provide MRD testing rely on a mix of internal budgets to run at-cost or at a lost, and charitable support. Patients may make co-payments to help fund the service. Because MRD testing can be also delivered as an outpatient service, out of pocket costs may apply to both private and public patients.

Provide at least one proposed item with their descriptor and associated costs, for each Population/Intervention:

Table 6 Proposed item, NGS

MBS item number (where used as a template for the proposed item)	73310
Category number	6
Category description	Pathology services
Proposed item descriptor	Measurable residual disease (MRD) testing by next-generation sequencing, performed on bone marrow from a patient diagnosed with multiple myeloma currently receiving active treatment, to confirm treatment response, or for disease monitoring to guide clinical management, as requested by a specialist or consultant physician practising as a haematologist or oncologist
Proposed MBS fee	100% = \$2,100.00

Indicate the overall cost per patient of providing the proposed health technology	\$2,100.00
Please specify any anticipated out of pocket expenses	\$0.00
Provide any further details and explain	

Table 7 Proposed item, flow cytometry

MBS item number (where used as a template for the proposed item)	71202
Category number	6
Category description	Pathology services
Proposed item descriptor	Measurable residual disease (MRD) testing by multiparametric flow cytometry to a minimum sensitivity of 10^{-5} performed on bone marrow from a patient diagnosed with multiple myeloma currently on active treatment, to confirm treatment response, or for disease monitoring to guide clinical management, as requested by a specialist or consultant physician practising as a haematologist or oncologist
Proposed MBS fee	100% = \$563.20
Indicate the overall cost per patient of providing the proposed health technology	\$563.20
Please specify any anticipated out of pocket expenses	\$0.00
Provide any further details and explain	

Algorithms

PREPARATION FOR USING THE HEALTH TECHNOLOGY

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:

The diagnostic workup of suspected MM includes various blood-based, urine and bone marrow tests to detect abnormalities in biochemical parameters to establish a diagnosis of MM. The 2014 IMWG guidelines state that a diagnosis of active MM must include both i) the presence of monoclonal plasma cells in the bone marrow $\geq 10\%$ or biopsy-proven bony or extramedullary plasmacytoma and 2) evidence of at least one SLiM-CRAB myeloma-defining event (International Myeloma Foundation 2026; Pires et al. 2025) described above in Table 1.

MRD testing is proposed in patients who achieve a complete response at key treatment milestones, defined according to the IMWG treatment response criteria. Current assessment of treatment response is multimodal. Multiple tests and services are used to determine treatment response and burden of disease. These include assessments of serum and urine M-protein, sFLC, bone marrow biopsy and advanced imaging (Table 4 and Table 5). These assessments represent routine care and are reimbursed through MBS items (outlined in the comparator section) and hospital funding. Not all tests and services may be ordered at the discretion of the physician. During maintenance therapy, patients are also regularly assessed with these tests and services for signs of relapse.

Is there any expectation that the clinical management algorithm before the health technology is used will change due to the introduction of the proposed health technology?

No

Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:

N/A

USE OF THE HEALTH TECHNOLOGY

Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:

A bone marrow aspirate is required for the purposes of MRD testing using NGS or NGF assays. MBS items relating to bone marrow biopsy and handling are MBS items 30081 and 30087. No other healthcare resources are required.

Explain what other healthcare resources are used in conjunction with the comparator health technology:

N/A

Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:

N/A

CLINICAL MANAGEMENT AFTER THE USE OF HEALTH TECHNOLOGY

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the proposed health technology

MRD testing is proposed following achievement of complete response, at key treatment milestones. In transplant-eligible patients, following an assessment of complete response, MRD testing is indicated post-induction, post-transplant, post-consolidation (if indicated), and at maintenance (Chen et al. 2026; Ramasamy et al. 2023).

If MRD-status is negative at post-induction, the depth of response suggests there is the potential option to defer transplant until relapse (Mo et al. 2023). Clinicians have indicated that stem cell transplant is considered mainstay therapy and it is likely that patients will proceed with the transplant as planned, however, patient preference may play a role in ASCT deferral. Studies in cancer patients highlights the importance of prognostic disclosure to inform decision-making (Chen and Tang 2014) and trade-off considerations between quality of life and length of life that are important to patients (Shrestha et al. 2019). Older patients for

example, may value quality of life over length of life, opting to forgo aggressive treatment (Shrestha et al. 2019). If MRD-status is positive post-transplant, treatment intensification could be considered (consolidation therapy), which could deepen response and result in superior health outcomes (Paiva et al. 2020). Similarly, MRD-positive status post-consolidation may indicate residual disease that requires further treatment. In maintenance, MRD-status can be used to guide the frequency and intensity of surveillance, with MRD-positivity indicating a higher risk of earlier relapse. On the other hand, MRD-negativity combined with achievement of complete response provides clinicians and patients with the confidence and reassurance in the depth of treatment response, which contributes to improved health outcomes (Munshi et al. 2020) and quality of life.

In transplant-ineligible patients, MRD testing is indicated following induction therapy after achievement of complete response, to inform whether further treatment intensification is required before proceeding to maintenance therapy (Chen et al. 2026). In maintenance, MRD-status can be used to guide the frequency and intensity of surveillance, with MRD-positivity indicating a higher risk of earlier relapse.

MRD testing is also proposed for disease monitoring during remission or maintenance therapy, every 6 months of patients with MRD-positive status and annually for patients with MRD-negative status aligned with international expert consensus (Chen et al. 2026).

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, after the use of the comparator health technology:

In the absence of MRD testing, patients achieving a complete response to treatment, continue with standard of care, either de-escalating treatment or proceeding to maintenance therapy. However, patients with residual disease would not be detected and risk early relapse without further treatment or intensification. During disease monitoring, the absence of MRD testing means that patients with positive MRD are not identified, reducing opportunities for early intervention and informed planning of subsequent treatment strategies before clinical relapse occurs. Conversely, patients with the deepest responses may not be provided the opportunity to stop or de-escalate therapy.

Describe and explain any differences in the healthcare resources used after the proposed health technology vs. the comparator health technology:

MRD testing may result in the treatment intensification of patients who are MRD-positive following achievement of complete response. In maintenance, patients with MRD-positivity can also be more closely monitored for relapse. MRD-negativity combined with achievement of complete response provides clinicians and patients with the confidence and reassurance in the depth of treatment response, which contributes to improved health outcomes and quality of life. A study published by Chen and Tang (2014) highlights the importance of prognostic disclosure to patients, supporting the value of prognostic information from MRD testing. Confirmed MRD-negativity alongside an assessment of complete response provides greater certainty in the depth of response, supporting clinician confidence in safely de-escalating or discontinuing therapy (Chen et al. 2026).

Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:

Figure 4 Current clinical management in transplant-eligible MM patients

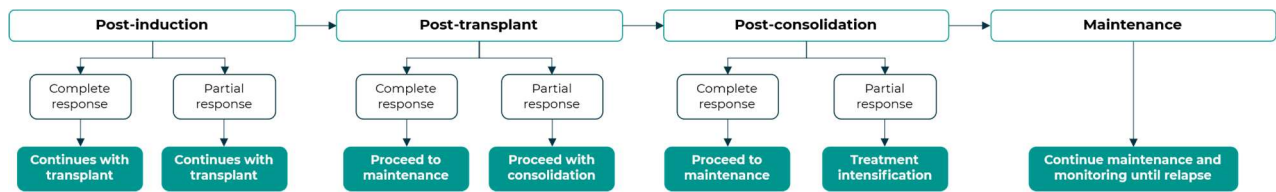
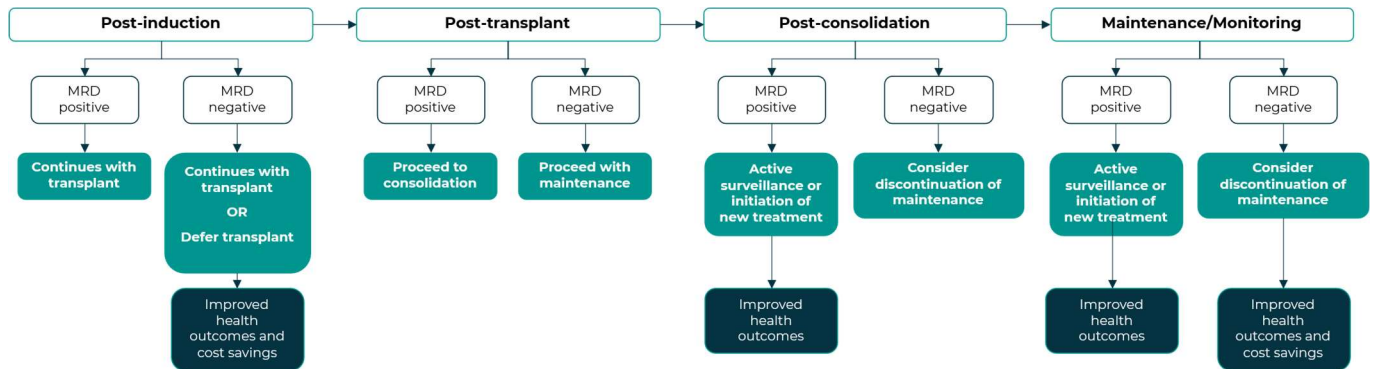


Figure 5 Proposed change in clinical management with MRD testing in transplant-eligible MM patients



Note: Treatment algorithm presents patients with CR by traditional methods

Figure 6 Current clinical management in transplant-ineligible MM patients

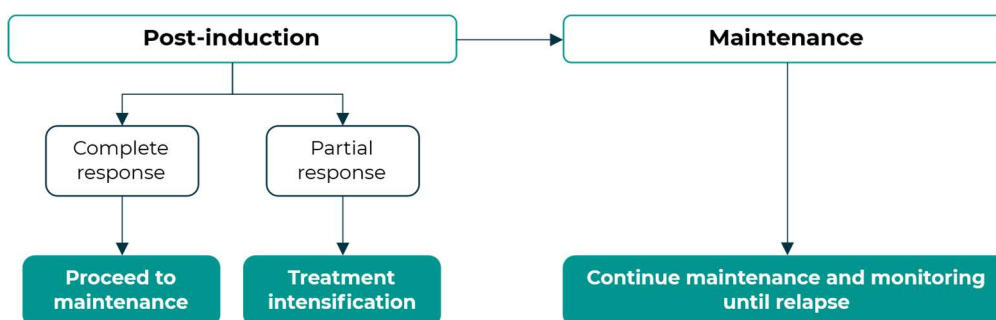
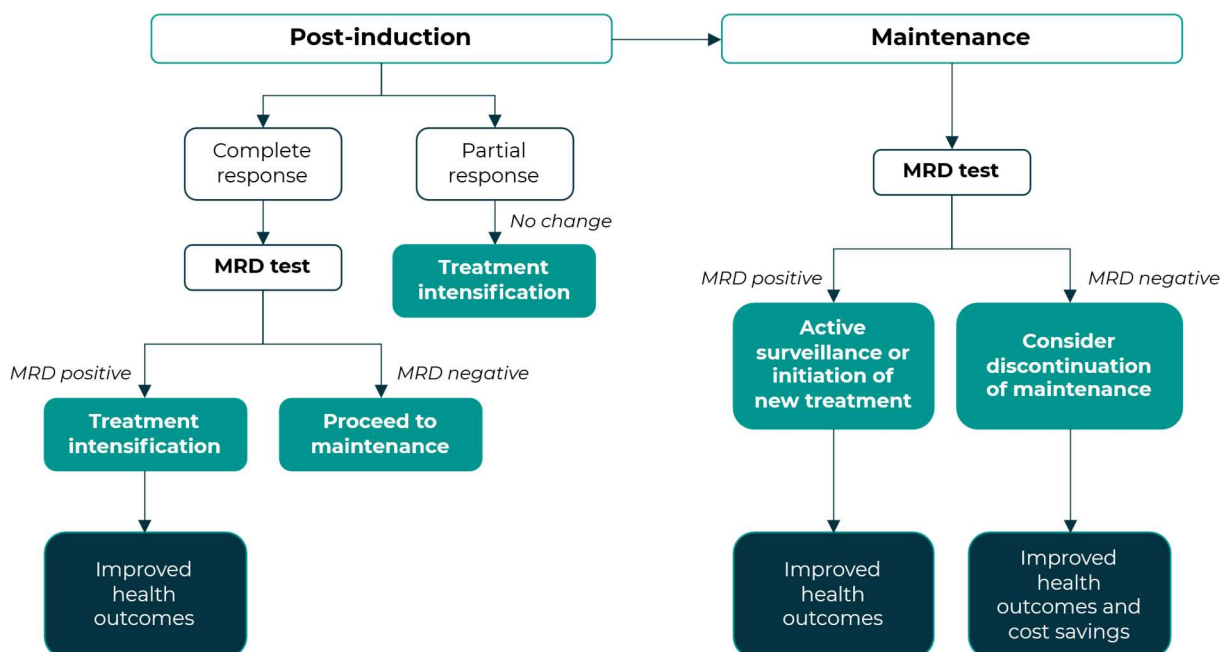


Figure 7 Proposed change in clinical management with MRD testing in transplant-ineligible MM patients



Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)?

(Please select your response)

- ☒ Superior
☐ Non-inferior
☐ Inferior

Please state what the overall claim is, and provide a rationale:

In comparison to current assessments of treatment response alone, MRD testing is claimed to result in superior health outcomes by enabling timely, and MRD-driven clinical management to improve PFS and OS.

In combination with an achievement of complete response, MRD-negativity is a strong prognostic indicator for PFS and OS and can serve as a clinical endpoint to guide treatment goals. Combined complete response and MRD-negativity can safely inform treatment de-escalation or discontinuation, avoid adverse events from treatment and improve quality of life.

Patients also benefit from the value of knowing the depth of treatment response and can feel reassured in treatment decisions.

In contrast, MRD-positivity despite an assessment of complete response is an indicator of persistent disease and increases the risk of early relapse. In such cases, the patient may benefit from seeking treatment intensification.

During monitoring, MRD testing can help to detect early disease resurgence allowing clinicians to adopt a dynamic risk-adapted strategy to prolong PFS.

Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?

MRD testing is a more precise measure of deeper response to treatment than traditional assessments. MRD provides additional prognostic information which is intended to complement standard assessments to holistically inform treatment decisions to improve patient outcomes.

Identify how the proposed technology achieves the intended patient outcomes:

MRD testing improves patient outcomes by providing a highly sensitive measure of disease burden that can identify residual myeloma cells undetectable by conventional assessments. MRD negativity is a strong predictor of improved PFS and OS), with meta-analyses demonstrating substantially better outcomes for patients who achieve MRD-negative status compared with those who remain MRD-positive (Munshi et al. 2020). Furthermore, deeper levels of MRD negativity (10^{-6}) and sustained MRD negativity over time are associated with the greatest survival benefits (Avet-Loiseau et al. 2021; Munshi et al. 2020). By providing accurate information on treatment response, MRD testing enables a risk-adapted approach to care, supporting treatment de-escalation or discontinuation in patients with sustained MRD negativity and treatment intensification in those with persistent MRD positivity. This personalised treatment strategy has the potential to improve long-term outcomes, reduce treatment-related toxicity, enhance quality of life, and optimise healthcare resource utilisation.

For some people, compared with the comparator(s), does the test information result in:

A change in clinical management?

Yes

A change in health outcome?

Yes

Other benefits?

Yes

Please provide a rationale, and information on other benefits if relevant:

MM is associated with significant treatment costs. While MM accounts for about 1% of all cancers in Australia, spending on pharmaceutical treatments for MM represents 11% of all PBS spend on cancer medicines in 2024-25 (PBAC 2026). By providing accurate and dynamic information on treatment response, MRD testing enables a risk-adapted approach to care, supporting treatment de-escalation or discontinuation in patients with sustained MRD negativity, optimising healthcare resource utilisation by providing cost-savings from treatment avoided.

In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator?

(Please select your response)

- ☒ More costly
☐ Same cost
☐ Less costly

Provide a brief rationale for the claim:

MRD testing is proposed as an adjunctive service and will not replace existing diagnostic services. MBS funding of MRD testing is therefore expected to increase the immediate costs to the MBS.

In the longer term, there are likely to be some cost offsets associated with more effective use of PBS listed therapies, following safe discontinuation of treatment guided by MRD results.

If your application is in relation to a specific radiopharmaceutical(s) or a set of radiopharmaceuticals, identify whether your clinical claim is dependent on the evidence base of the radiopharmaceutical(s) for which MBS funding is being requested. If your clinical claim is dependent on the evidence base of another radiopharmaceutical product(s), a claim of clinical noninferiority between the radiopharmaceutical products is also required.

N/A

Summary of Evidence

Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology. At 'Application Form lodgement',

	Type of study design*	Title of journal article or research project <i>(including any trial identifier or study lead if relevant)</i>	Short description of research <i>(max 50 words)**</i>	Website link to journal article or research <i>(if available)</i>	Date of publication <i>***</i>
1.	Pooled analysis of clinical trials	Depth of Response in Multiple Myeloma: A Pooled Analysis of Three PETHEMA/GEM Clinical Trials [PANTHEMA/GEM]	This study supports MRD-negativity as a strong prognostic marker, with greater prognostic value than traditional haematological response measures such as	https://pubmed.ncbi.nlm.nih.gov/28498784/	Lahuerta et al. (2017) 12/05/2017

			complete response.		
2	Retrospective real world study	Role of clonoSEQ®, a Next-Generation Sequencing (NGS) Assay and PET As a Measure of Minimal Residual Disease Negativity Among Patients with Multiple Myeloma	MRD-negativity was associated with longer PFS and OS across patient subgroups and showed greater prognostic discrimination than complete response. Higher MRD-negative rates after induction predicted longer PFS, regardless of regimen.	https://ashpublications.org/blood/article/136/Supplement%201/50/471353/Role-of-clonoSEQ-a-Next-Generation-Sequencing-NGS	Nooka et al. (2020) 05/11/2020
3	Phase III clinical trial	Measurable Residual Disease–Guided Therapy in Newly	The study shows that MRD testing can be used to inform the	https://www.nejm.org/doi/10.1056/NEJMoa2505133	Perrot et al. (2025) 03/06/2025

		Diagnosed Myeloma [MIDAS]	discontinuation on maintenance treatment (with daratumumab).		
4 .	Phase II clinical trial	Discontinuation of maintenance therapy in multiple myeloma guided by multimodal measurable residual disease negativity [MRD2STOP]	Daratumumab maintenance was stopped after at least 24 months if patients sustained MRD-negativity for at least 12 months. Overall, 64% discontinued maintenance after sustained MRD-negativity.	https://pubmed.ncbi.nlm.nih.gov/39375362/	Derman et al. (2024) 07/10/2024
5 .	Phase II clinical trial	Defining the Optimal Duration of Lenalidomide Maintenance	The study demonstrated that MRD-guided lower intensive	https://ashpublications.org/blood/article/140/Supplement%201/1371/491394/Defining-the-Optimal-Duration-of-Lenalidomide	Pawlyn et al. (2022) 15/11/2022

		after Autologous Stem Cell Transplant - Data from the Myeloma XI Trial [MYELOMA XI]	consolidation therapy was able to achieve comparable health outcomes in the high-intensity group, avoiding exposure to toxicity of treatment and adverse effects while maintaining treatment benefit.		
6 .	Phase II clinical trial	Phase 2 Study Using Minimal Residual Disease-Driven Adaptive Strategy in Newly Diagnosed Multiple Myeloma with Upfront Daratumumab-Based Therapy -	MRD-negative patients achieved similar outcomes with lower-intensity treatment. MRD-guided consolidation showed no significant	https://ashpublications.org/blood/article/144/Supplement%201/3379/533918/Phase-2-Study-Using-Minimal-Residual-Disease	Ye et al. (2024) 05/11/2024

		First Report from the Maestro Trial [MAESTRO]	advantage for ASCT over Isa-KRd after induction, or for tandem ASCT over single ASCT plus Isa-KRd in MRD-positive patients.		
7 .	Phase II clinical trial	Elotuzumab and Weekly Carfilzomib, Lenalidomide, and Dexamethasone in Patients With Newly Diagnosed Multiple Myeloma Without Transplant Intent: A Phase 2 Measurable Residual Disease-Adapted Study [NCT02969837]	The study demonstrated that maintenance therapy could be safely stopped among patients with MRD-negative status who had received at least 1 year of therapy.	https://pubmed.ncbi.nlm.nih.gov/35862034/	Derman et al. (2022) 01/09/2022

8	Phase II clinical trial	Minimal residual disease response-adapted therapy in newly diagnosed multiple myeloma (MASTER): final report of the multicentre, single-arm, phase 2 trial [MASTER]	Patients were on maintenance therapy for a median of 36 months (12-95 months) before cessation. Discontinuation of maintenance therapy with multimodal MRD-negativity resulted in low rates of disease resurgence or progression.	https://pubmed.ncbi.nlm.nih.gov/37776872/	Costa et al. (2023) 27/09/2023
9	Phase III clinical study	Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma [PERSEUS]	Addition of daratumumab to VRd significantly increased MRD-negative rates (75.2% vs 47.5%) in	https://www.nejm.org/doi/full/10.1056/NEJMoa2312054	Sonneveld et al. (2024) 12/12/2024

			transplant-eligible newly diagnosed multiple myeloma and was associated with improved progression-free survival. These findings support achieving deep MRD-negativity as an important treatment outcome and prognostic marker.		
--	--	--	--	--	--

* Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.

** Provide high level information including population numbers and whether patients are being recruited or in post-recruitment, including providing the trial registration number to allow for tracking purposes. For yet to be published research, provide high level information including population numbers and whether patients are being recruited or in post-recruitment.

*** If the publication is a follow-up to an initial publication, please advise. For yet to be published research, include the date of when results will be made available (to the best of your knowledge).

Identify yet-to-be-published research that may have results available in the near future (that could be relevant to your application).

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
1.	Phase II clinical trial	REMNANT	This ongoing study assesses whether treating at first MRD relapse improves survival compared with waiting for clinical or biochemical relapse. Patients with NDMM are followed during first-line treatment, with MRD-negative patients eligible for randomisation.	https://clinicaltrials.gov/study/NCT04513639	NCT04513639 20/03/2025

* Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.

** Provide high level information including population numbers and whether patients are being recruited or in post-recruitment, including providing the trial registration number to allow for tracking purposes. For yet to be published research, provide high level information including population numbers and whether patients are being recruited or in post-recruitment.

*** If the publication is a follow-up to an initial publication, please advise. For yet to be published research, include the date of when results will be made available (to the best of your knowledge).

References

- Avet-Loiseau H, J San-Miguel, T Casneuf, S Iida, S Lonial, SZ Usmani, A Spencer, P Moreau, T Plesner, K Weisel, J Ukropec, C Chiu, S Trivedi, H Amin, M Krevvata, P Ramaswami, X Qin, M Qi, S Sun, M Qi, R Kobos and NJ Bahlis (2021). Evaluation of Sustained Minimal Residual Disease Negativity With Daratumumab-Combination Regimens in Relapsed and/or Refractory Multiple Myeloma: Analysis of POLLUX and CASTOR. *J Clin Oncol* 39(10): 1139–1149.DOI: 10.1200/jco.20.01814
- Bain BJ (2005). Bone marrow biopsy morbidity: review of 2003. *J Clin Pathol* 58(4): 406–408.DOI: 10.1136/jcp.2004.022178
- Binding Site (2026) Monoclonal gammopathies and multiple myeloma. Challenges with traditional monitoring. Accessible at <https://www.thermofisher.com/bindingsite/wo/en/clinical-applications/monoclonal-gammopathies/challenges-with-traditional-monitoring.html>
- Bio-Rad Laboratories Inc (2026). *Flow Cytometry Standardization — Best Practices, Calibration, and Validation Reagents*. Accessed 15 July 2026. <https://www.bio-rad-antibodies.com/flow-cytometry-calibration-validation-reagents.html>
- Biocompare (15 August 2023). Flow Cytometry Principles, Protocol Steps, and Practical Tips. Accessed 15 July 2026 <https://www.biocompare.com/Editorial-Articles/598332-Flow-Cytometry-Principles-Protocol-Steps-and-Practical-Tips/>
- Brinkman RR (2020). Improving the Rigor and Reproducibility of Flow Cytometry-Based Clinical Research and Trials Through Automated Data Analysis. *Cytometry A* 97(2): 107–112.DOI: 10.1002/cyto.a.23883
- Cancer Australia (18 December 2025). Multiple myeloma in Australia statistics. Australian Government. Accessed 23 June 2026 <https://www.canceraustralia.gov.au/cancer-types/myeloma/multiple-myeloma-australia-statistics>
- Cancer Council (2026). *Multiple myeloma. Your guide to best cancer care*. Accessed 14 July 2026. <https://www.cancer.org.au/cancercareguides/multiple-myeloma>
- Cassano RC, R Banerjee, A Afrough, AJ Portuguese, R Thakur, K Cicero, M Kwok, L Foster, G Buda, S Meletath, S Galimberti, G Serviddio, MV Dhodapkar and D Dima (2026). MRD in multiple myeloma: Moving from “minimal” to “measurable”. *Blood Reviews*: 101413.DOI: <https://doi.org/10.1016/j.blre.2026.101413>
- Chen C-H and S-T Tang (2014). Prognostic Disclosure and its Influence on Cancer Patients. *Journal of Cancer Research and Practice* 1(2): 103–112.DOI: <https://doi.org/10.6323/JCRP.2014.1.2.02>
- Chen W, Z Cai, CS Chim, WJ Chng, J Du, C Fu, W Gao, I Hanamura, J Hou, JS-Y Huang, T Ishida, C Li, A Liu, V Ptushkin, N Takezako, RSM Wong and DH Yoon (2026). Guidelines and consensus for minimal residual disease-adapted therapy in multiple myeloma from the {Pan}-{Pacific} multiple myeloma working group. *Clinical Hematology International* 8(2): 7–25.DOI: 10.46989/001c.160933
- Chim CS, SK Kumar, RZ Orlowski, G Cook, PG Richardson, MA Gertz, S Giral, MV Mateos, X Leleu and KC Anderson (2018). Management of relapsed and refractory multiple myeloma: novel agents, antibodies, immunotherapies and beyond. *Leukemia* 32(2): 252–262.DOI: 10.1038/leu.2017.329
- Ching T, ME Duncan, T Newman-Eerkes, MME McWhorter, JM Tracy, MS Steen, RP Brown, S Venkatasubbarao, NK Akers, M Vignali, ME Moorhead, D Watson, RO Emerson, TP Mann, BM Cimler, PL Swatkowski, IR Kirsch, C Sang, HS Robins, B Howie and A Sherwood (2020). Analytical evaluation of the clonoSEQ Assay for establishing measurable (minimal) residual disease in acute lymphoblastic leukemia, chronic lymphocytic leukemia, and multiple myeloma. *BMC Cancer* 20(1): 612.DOI: 10.1186/s12885-020-07077-9
- Costa LJ, S Chhabra, E Medvedova, BR Dholaria, TM Schmidt, KN Godby, R Silbermann, B Dhakal, S Bal, S Giri, A D'Souza, AC Hall, P Hardwick, J Omel, RF Cornell, P Hari and NS Callander (2023). Minimal residual disease response-adapted therapy in newly diagnosed multiple myeloma (MASTER): final report of the multicentre, single-arm, phase 2 trial. *Lancet Haematol* 10(11): e890–e901.DOI: 10.1016/s2352-3026(23)00236-3

Dejoie T, D Lakomy, H Caillon, B Pegourié and O Decaux (2016). IFM (Intergroupe francophone du myélome) recommendations for uniform interpretation of serum and urine protein electrophoresis in multiple myeloma diagnosis and follow-up. *Ann Biol Clin (Paris)* 74(4): 429–441.DOI: 10.1684/abc.2016.1166

Derman BA, A Kansagra, J Zonder, AT Stefka, DL Grinblatt, LD Anderson, Jr., S Gurbuxani, S Narula, S Rayani, A Major, A Kin, K Jiang, T Karrison, J Jasielec and AJ Jakubowiak (2022). Elotuzumab and Weekly Carfilzomib, Lenalidomide, and Dexamethasone in Patients With Newly Diagnosed Multiple Myeloma Without Transplant Intent: A Phase 2 Measurable Residual Disease-Adapted Study. *JAMA Oncol* 8(9): 1278–1286.DOI: 10.1001/jamaoncol.2022.2424

Derman BA, A Major, J Cooperrider, K Jiang, A Ramsland, T Karrison, T Kubicki and AJ Jakubowiak (2024). Discontinuation of maintenance therapy in multiple myeloma guided by multimodal measurable residual disease negativity (MRD2STOP). *Blood Cancer J* 14(1): 170.DOI: 10.1038/s41408-024-01156-x

Dimopoulos MA, AJ Jakubowiak, PL McCarthy, RZ Orlowski, M Attal, J Bladé, H Goldschmidt, KC Weisel, K Ramasamy, S Zweegman, A Spencer, JSY Huang, J Lu, K Sunami, S Iida, WJ Chng, SA Holstein, A Rocci, T Skacel, R Labotka, A Palumbo and KC Anderson (2020). Developments in continuous therapy and maintenance treatment approaches for patients with newly diagnosed multiple myeloma. *Blood Cancer J* 10(2): 17.DOI: 10.1038/s41408-020-0273-x

Eslick R and D Talaulikar (October 2013). Multiple myeloma: from diagnosis to treatment. Australian Family Practice. <https://www.racgp.org.au/afp/2013/october/multiple-myeloma>

Facon T, S Kumar, T Plesner, RZ Orlowski, P Moreau, N Bahlis, S Basu, H Nahi, C Hulin, H Quach, H Goldschmidt, M O'Dwyer, A Perrot, CP Venner, K Weisel, JR Mace, N Raje, M Attal, M Tiab, M Macro, L Frenzel, X Leleu, T Ahmadi, C Chiu, J Wang, RV Rampelbergh, CM Uhlar, R Kobos, M Qi and SZ Usmani (2019). Daratumumab plus Lenalidomide and Dexamethasone for Untreated Myeloma. *New England Journal of Medicine* 380(22): 2104–2115.DOI: doi:10.1056/NEJMoa1817249

FDA (2020). K200009 510(k) substantial equivalence determination decision summary U. F. D. Administration.

Flores-Montero J, L Sanoja-Flores, B Paiva, N Puig, O García-Sánchez, S Böttcher, VHJ van der Velden, JJ Pérez-Morán, MB Vidriales, R García-Sanz, C Jimenez, M González, J Martínez-López, A Corral-Mateos, GE Grigore, R Fluxá, R Pontes, J Caetano, L Sedek, MC Del Cañizo, J Bladé, JJ Lahuerta, C Aguilar, A Báez, A García-Mateo, J Labrador, P Leoz, C Aguilera-Sanz, J San-Miguel, MV Mateos, B Durie, JJM van Dongen and A Orfao (2017). Next Generation Flow for highly sensitive and standardized detection of minimal residual disease in multiple myeloma. *Leukemia* 31(10): 2094–2103.DOI: 10.1038/leu.2017.29

Gerlach A (17 September 2025). Updated IMWG Guidelines Spotlight MRD, Functional Imaging, and Light Chain Assays in Multiple Myeloma. Pharmacy times. Accessed 24 June 2026 <https://www.pharmacytimes.com/view/updated-imwg-guidelines-spotlight-mrd-functional-imaging-and-light-chain-assays-in-multiple-myeloma>

Grossman J and K Crumrin (6 January 2026). Multiple myeloma maintenance therapy: 6 Facts. MyMyelomaTeam website. Accessed 17 July 2026 <https://www.mymyelomateam.com/resources/5-things-to-know-about-multiple-myeloma-maintenance-therapy>

Ho M and T Kourelis (2022). The burden of myeloma: novel approaches to disease assessment. *Hematology* 2022(1): 356–362.DOI: 10.1182/hematology.2022000348

International Myeloma Foundation (12 July 2026). Multiple Myeloma Diagnostic Criteria. Accessed 14 July 2026 <https://www.myeloma.org/newly-diagnosed/multiple-myeloma-diagnostic-criteria>

Jung J (2025). Treatment of transplant-ineligible multiple myeloma. *Blood Res* 60(1): 53.DOI: 10.1007/s44313-025-00102-5

Kumar S, S Jacobus, A Cohen, M Weiss, N Callander, A Singh, T Parker, M Green, R Thertulien, B Parsons, P Kumar, P Kapoor, A Rosenberg, E Dib, D Almquist, J Zonder, E Faber, Z Wei, K Anderson, S Lonial, P Richardson, R Orlowski, L Wagner and SV Rajkumar (2026). Continuous or Fixed-Duration Maintenance Therapy in Multiple Myeloma. *New England Journal of Medicine* 395(3): 221–232.DOI: doi:10.1056/NEJMoa2600157

Kumar S, B Paiva, KC Anderson, B Durie, O Landgren, P Moreau, N Munshi, S Lonial, J Bladé, M-V Mateos, M Dimopoulos, E Kastritis, M Boccadoro, R Orlowski, H Goldschmidt, A Spencer, J Hou, WJ Chng, SZ Usmani, E Zamagni, K Shimizu, S Jagannath, HE Johnsen, E Terpos, A Reiman, RA Kyle, P Sonneveld, PG Richardson, P McCarthy, H Ludwig, W Chen, M Cavo, J-L Harousseau, S Lentzsch, J Hillengass, A Palumbo, A Orfao, SV Rajkumar, JS Miguel and H Avet-Loiseau (2016). International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. *The Lancet Oncology* 17(8): e328–e346.DOI: [https://doi.org/10.1016/S1470-2045\(16\)30206-6](https://doi.org/10.1016/S1470-2045(16)30206-6)

Lahuerta JJ, B Paiva, MB Vidriales, L Cerdón, MT Cedena, N Puig, J Martinez-Lopez, L Rosiñol, NC Gutierrez, ML Martín-Ramos, A Oriol, AI Teruel, MA Echeveste, R de Paz, F de Arriba, MT Hernandez, L Palomera, R Martinez, A Martin, A Alegre, J De la Rubia, A Orfao, MV Mateos, J Blade and JF San-Miguel (2017). Depth of Response in Multiple Myeloma: A Pooled Analysis of Three PETHEMA/GEM Clinical Trials. *J Clin Oncol* 35(25): 2900–2910.DOI: 10.1200/jco.2016.69.2517

Martinez-Lopez J, N Lopez-Muñoz, A Chari, S Dorado, S Barrio, S Arora, A Kumar, A Chung, T Martin and J Wolf (2024). Measurable residual disease (MRD) dynamics in multiple myeloma and the influence of clonal diversity analyzed by artificial intelligence. *Blood Cancer J* 14(1): 131.DOI: 10.1038/s41408-024-01102-x

Martino EA, E Vigna, C Labanca, A Bruzzese, F Mendicino, G Caridà, E Lucia, V Olivito, N Puccio, N Amodio, A Neri, F Morabito and M Gentile (2025). Maintenance therapy after ASCT in newly diagnosed multiple myeloma patients: single agent versus combination drugs. *Expert Rev Hematol* 18(9): 719–734.DOI: 10.1080/17474086.2025.2525457

McKinnon KM (2018). Flow Cytometry: An Overview. *Curr Protoc Immunol* 120: 5.1.1–5.1.11.DOI: 10.1002/cpim.40

Meseha M, J Hoffman, D Kazandjian, O Landgren and B Diamond (2024). Minimal Residual Disease-Adapted Therapy in Multiple Myeloma: Current Evidence and Opinions. *Current Oncology Reports* 26(6): 679–690.DOI: 10.1007/s11912-024-01537-2

MMRF (2026). MULTIPLE MYELOMA AUTOLOGOUS STEM CELL TRANSPLANTATION. Multiple Myeloma Research Foundation.

Mo CC, MA Hartley-Brown, S Midha and PG Richardson (2023). Upfront or Deferred Autologous Stem Cell Transplantation for Newly Diagnosed Multiple Myeloma in the Era of Triplet and Quadruplet Induction and Minimal Residual Disease/Risk-Adapted Therapy. *Cancers (Basel)* 15(24).DOI: 10.3390/cancers15245709

Munshi NC, H Avet-Loiseau, KC Anderson, P Neri, B Paiva, M Samur, M Dimopoulos, M Kulakova, A Lam, M Hashim, J He, B Heeg, J Ukropec, J Vermeulen, S Cote and N Bahlis (2020). A large meta-analysis establishes the role of MRD negativity in long-term survival outcomes in patients with multiple myeloma. *Blood Adv* 4(23): 5988–5999.DOI: 10.1182/bloodadvances.2020002827

Myeloma Australia (2026a). Clinical practice guideline. Management of patients with newly diagnosed multiple myeloma who are eligible for autologous stem cell transplantation. M. S. A. G. t. M. Australia.

Myeloma Australia (2026b). Clinical practice guideline. Treatment of patients with newly diagnosed multiple myeloma who are ineligible for autologous stem cell transplantation.

Myeloma Australia (2026c). Clinical practice guideline. Treatment of patients with relapsed refractory multiple myeloma.

Myeloma Australia (2026d) Clinical Practice Guidelines. Accessible at <https://myeloma.org.au/health-professionals/guidelines-education/clinical-practice-guidelines/>

NCCN (National Comprehensive Cancer Network) (2026). *Multiple myeloma clinical guidelines. Response criteria for multiple myeloma*. Accessed 23 July 2026. https://guidelines.nccn.org/guidelines/myeloma?_session=6319E4113376019A64A7B064A127EC05

Nooka A, K Bradley, N Joseph, CC Hofmeister, MV Dhodapkar, LH Boise, S Lonial, S Li and JL Kaufman (2020). Role of clonoSEQ®, a Next-Generation Sequencing (NGS) Assay and PET/CT As a Measure of Minimal Residual Disease Negativity Among Patients with Multiple Myeloma. *Blood* 136(Supplement 1): 50–51.DOI: 10.1182/blood-2020-143093

Padala SA, A Barsouk, A Barsouk, P Rawla, A Vakiti, R Kolhe, V Kota and GH Ajebo (2021). Epidemiology, Staging, and Management of Multiple Myeloma. *Med Sci (Basel)* 9(1).DOI: 10.3390/medsci9010003

Paiva B, N Puig, M-T Cedena, L Rosiñol, L Cerdón, M-B Vidriales, L Burgos, J Flores-Montero, L Sanoja-Flores, L Lopez-Anglada, R Maldonado, Jdl Cruz, NC Cutierrez, M-J Calasanz, M-L Martin-Ramos, R Garcia-Sanz, J Martinez-Lopez, A Oriol, M-J Blanchard, R Rios, J Martin, R Martinez-Martinez, A Sureda, M-T Hernandez, Jdl Rubia, I Krsnik, J-M Moraleda, L Palomera, J Bargay, JJMV Dongen, A Orfao, M-V Mateos, J Blade, JF San-Miguel and J-J Lahuerta (2020). Measurable Residual Disease by Next-Generation Flow Cytometry in Multiple Myeloma. *Journal of Clinical Oncology* 38(8): 784–792.DOI: 10.1200/jco.19.01231

Paiva B, J San-Miguel and H Avet-Loiseau (2022). MRD in multiple myeloma: does CR really matter? *Blood* 140(23): 2423–2428.DOI: 10.1182/blood.2022016170

Pawlyn C, T Menzies, FE Davies, RM de Tute, R Henderson, G Cook, MW Jenner, JR Jones, MF Kaiser, MT Drayson, RG Owen, D Cairns, GJ Morgan and G Jackson (2022). Defining the Optimal Duration of Lenalidomide Maintenance after Autologous Stem Cell Transplant - Data from the Myeloma XI Trial. *Blood* 140(Supplement 1): 1371–1372.DOI: 10.1182/blood-2022-165376

PBAC (2026). *Multiple Myeloma Stakeholder Meeting (Sponsors). Outcome Statement*. The Pharmaceutical Benefits Advisory Committee. Accessed 3 February 2026. <https://pbs.gov.au/industry/listing/elements/pbac-meetings/pbac-stakeholder-meetings/Multiple-Myeloma-Sponsor-Outcomes-Statement-February-2026.pdf>

Perrot A, J Lambert, C Hulin, A Pieragostini, L Karlin, B Arnulf, P Rey, L Garderet, M Macro, M Escoffre-Barbe, J Gay, T Chalopin, R Gounot, J-M Schiano, M Mohty, X Leleu, S Manier, C Mariette, C Chaletex, T Braun, B De Pijck, H Avet-Loiseau, J-Y Mary, J Corre, P Moreau and C Touzeau (2025). Measurable Residual Disease–Guided Therapy in Newly Diagnosed Myeloma. *New England Journal of Medicine* 393(5): 425–437.DOI: 10.1056/NEJMoa2505133

Perrot A, V Lauwers-Cances, J Corre, N Robillard, C Hulin, ML Chretien, T Dejoie, S Maheo, AM Stoppa, B Pegourie, L Karlin, L Garderet, B Arnulf, C Doyen, N Meuleman, B Royer, JR Eveillard, L Benboubker, M Dib, O Decaux, A Jaccard, K Belhadj, S Brechignac, B Kolb, C Fohrer, M Mohty, M Macro, PG Richardson, V Carlton, M Moorhead, T Willis, M Faham, KC Anderson, JL Harousseau, X Leleu, T Facon, P Moreau, M Attal, H Avet-Loiseau and N Munshi (2018). Minimal residual disease negativity using deep sequencing is a major prognostic factor in multiple myeloma. *Blood* 132(23): 2456–2464.DOI: 10.1182/blood-2018-06-858613

PeterMac (P. M. C. Centre)). Biopsies - including Bone Marrow Biopsy. Accessed 14 July 2026 <https://www.petermac.org/patients-and-carers/tests-and-diagnosis/biopsies-including-bone-marrow-biopsy>

Pires AM, JP Barreto, J Caetano, MJ Soares, C Geraldles, B Fernandes, M Coucelo, S Chacim, H Coelho, C Correia, AP Cruz, M Cunha, MR Cunha, N Cunha, P Ferraz, JG Freitas, R Henrique, S Lisboa, P Lúcio, A Paiva, C Pedrosa, I Ramos, AB Sarmiento-Ribeiro, P Seabra, J Sevilha, MJR Sousa, S Sousa, T Sousa, M Tavares, F Trigo, A Roque, R Bergantim, C João and G On Behalf Of The Portuguese Multiple Myeloma (2025). Multiple Myeloma Laboratory Diagnostics Made Simple: Practical Insights and Key Recommendations. *J Clin Med* 14(19).DOI: 10.3390/jcm14197115

Popat R, A Oriol, M Cavo, L Karlin, I Avivi Mazza, W Roeloffzen, SJ Kim, B Lipe, N Bar, N Horvath, A Spencer, C-K Min, D Chen, Q Li, K Li, A Slaughter, C Lonardi, N Benachour, A Ghosh, M Vogel, N Lendvai, T Lengil, N Patel, O Costa Filho, E Florendo and Y Lin (2024). Ciltacabtagene Autoleucel (Cilta-cel) Vs Standard of Care (SoC) in Patients with Lenalidomide (Len)-Refractory Multiple Myeloma (MM) after 1-3 Lines of Therapy: Minimal Residual Disease (MRD) Negativity in the Phase 3 Cartitude-4 Trial. *Blood* 144(Supplement 1): 1032–1032.DOI: 10.1182/blood-2024-201533

Quach HP, HM. Harrison, S. (2022). Clinical Practice Guideline Multiple Myeloma, Myeloma Australia.

Ramasamy K, H Avet-Loiseau, C Hveding Blimark, M Delforge, F Gay, S Manier, J Martinez-Lopez, MV Mateos, M Mohty, N van de Donk and K Weisel (2023). Measurable Residual Disease Testing in Multiple Myeloma Routine Clinical Practice: A Modified Delphi Study. *Hemasphere* 7(9): e942.DOI: 10.1097/hs9.0000000000000942

Robinson JP, GB Gmyrek and B Rajwa (2026). Flow Cytometry: Advances, Challenges and Trends. *Bioessays* 48(1): e70091.DOI: 10.1002/bies.70091

Rodríguez-Lobato LG, A de Daniel, A Pereira, C Fernández de Larrea, N Tovar, MT Cibeira, DF Moreno, JM Mateos, N Llobet, E Carcelero, D Munárriz, J Bladé and L Rosiñol (2025). Attrition rates and treatment outcomes in multiple myeloma: real-world data over a 40-year period. *Blood Cancer J* 15(1): 103.DOI: 10.1038/s41408-025-01311-y

Shrestha A, C Martin, M Burton, S Walters, K Collins and L Wyld (2019). Quality of life versus length of life considerations in cancer patients: A systematic literature review. *Psychooncology* 28(7): 1367–1380.DOI: 10.1002/pon.5054

Sonneveld P, A Dimopoulos Meletios, M Boccadoro, H Quach, PJ Ho, M Beksac, C Hulin, E Antonioli, X Leleu, S Mangiacavalli, A Perrot, M Cavo, A Belotti, A Broijl, F Gay, R Mina, S Nijhof Inger, WCJ van de Donk Niels, E Katodritou, F Schjesvold, A Sureda Balari, L Rosiñol, M Delforge, W Roeloffzen, T Silzle, A Vangsted, H Einsele, A Spencer, R Hajek, A Jurczynszyn, S Lonergan, T Ahmadi, Y Liu, J Wang, D Vieyra, MJ van Brummelen Emilie, V Vanquickenberghe, A Sitthi-Amorn, J de Boer Carla, R Carson, P Rodriguez-Otero, J Bladé and P Moreau (2024). Daratumumab, Bortezomib, Lenalidomide, and Dexamethasone for Multiple Myeloma. *New England Journal of Medicine* 390(4): 301–313.DOI: 10.1056/NEJMoa2312054

Szalat R (5 March 2026). Minimal Residual Disease Testing in Multiple Myeloma. ASCO Daily news. Accessed 29 June 2026 <https://dailynews.ascopubs.org/doi/minimal-residual-disease-testing-multiple-myeloma>

Urushihara R, N Takezako, T Yoroidaka, T Yamashita, R Murata, K Satou, S Nakao and H Takamatsu (2023). Eight-color multiparameter flow cytometry (EuroFlow-NGF) is as sensitive as next-generation sequencing in detecting minimal/measurable residual disease in autografts of patients with multiple myeloma. *EJHaem* 4(1): 184–191.DOI: 10.1002/jha2.633

Wijnands C, S Noori, NWCJvd Donk, MM VanDuijn and JFM Jacobs (2023). Advances in minimal residual disease monitoring in multiple myeloma. *Critical Reviews in Clinical Laboratory Sciences* 60(7): 518–534.DOI: 10.1080/10408363.2023.2209652

Yan W, J Xu, H Fan, L Li, J Cui, C Du, S Deng, W Sui, Y Xu, M Hao, KC Anderson, D Zou, L Qiu and G An (2024). Early relapse within 18 months is a powerful dynamic predictor for prognosis and could revise static risk distribution in multiple myeloma. *Cancer* 130(3): 421–432.DOI: 10.1002/cnrcr.35056

Ye JC, P Boonstra, EL Campagnaro, M Pianko, A Kin, LD Anderson, Jr., B Lipe, M Talpaz and JA Zonder (2024). Phase 2 Study Using Minimal Residual Disease-Driven Adaptive Strategy in Newly Diagnosed Multiple Myeloma with Upfront Daratumumab-Based Therapy - First Report from the Maestro Trial. *Blood* 144(Supplement 1): 3379–3379.DOI: 10.1182/blood-2024-209505

Yee AJ and N Raje (2021). Minimal residual disease in multiple myeloma: why, when, where. *Hematology* 2021(1): 37–45.DOI: 10.1182/hematology.2021000230

Zabaleta A, N Puig, MT Cedena, A Oliver-Caldes, JJ Perez, C Moreno, LE Tamariz-Amador, P Rodriguez-Otero, F Prosper, V Gonzalez-Calle, L López-Corral, B Rey-Búa, B Puertas, F Mirás, JM Sánchez-Pina, N López-Muñoz, M Juan, EA González-Navarro, Á Urbano, CF de Larrea, J Blade, JJ Lahuerta, J Martinez-Lopez, MV Mateos, JF San Miguel and B Paiva (2025). Clinical significance of complete remission and measurable residual disease in relapsed/refractory multiple myeloma patients treated with T-cell redirecting immunotherapy. *Am J Hematol* 100(1): 93–102.DOI: 10.1002/ajh.27526

Zhou Q-Y, J-L Song, X Wu, K Qian, L-L Hu, X-Y Ma, J-M Zhou, J-J Zhu, M Aimaiti, R-T Huang, Q Zhou, Y-T Zhang, M Guan, Y Lin and S-Y Chen (2026). Advances in flow cytometry: technological innovations and their expanding role in biomedical research and clinical practice. *LabMed Discovery* 3(1): 100116.DOI: <https://doi.org/10.1016/j.lmd.2026.100116>