

MSAC Application 1831

Kappa free-light chain (kFLC) index testing for the diagnosis of multiple sclerosis (MS)

PICO Set

Population

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

Kappa free-light chain (kFLC) index testing is a paraclinical test in patients undergoing diagnostic assessment for suspected multiple sclerosis (MS), where evidence of intrathecal immunoglobulin synthesis is required to support diagnosis.¹

MS is a chronic, immune-mediated neurodegenerative disease of the central nervous system (CNS), characterised by inflammation, demyelination and gliosis within the white and grey matter of the brain and spinal cord, forming plaques or lesions.² Early disease, including clinically isolated syndrome (CIS) and relapsing-remitting MS (RRMS), is dominated by active inflammatory demyelination with lymphocyte infiltration, B cell activity, macrophage/microglial activation and reactive gliosis. In primary or secondary progressive MS, lesions are more often chronic and inactive, with established demyelination, axonal loss, astrocytic gliosis and persistent compartmentalised CNS inflammation, including meningeal immune aggregates.^{2,3} A characteristic feature of MS is intrathecal immunoglobulin synthesis, which is why (CSF) biomarkers such as oligoclonal bands (OCB) and kFLC are used as supportive evidence in the diagnosis of MS.

MS is commonly diagnosed between 20 and 40 years of age and is a leading cause of non-traumatic physical and cognitive disability in young adults. The inflammatory disease activity and neurodegeneration caused by MS leads to varied neurological symptoms, cumulative disability, reduced quality of life and workforce participation, and long-term need for multidisciplinary care. In Australia, an estimated 37,756 people were living with MS in 2024, a 77% increase since 2010, with total annual economic burden exceeding \$3.0 billion.^{3,4}

Establishing an accurate diagnosis of MS can be challenging as there is no single definitive test, and the disease can mimic other inflammatory, infectious, vascular, metabolic, structural or functional neurological conditions. Timely diagnosis supports earlier treatment while reducing the risk of misdiagnosis and inappropriate therapy in people with alternative conditions, both of which are critical in a disease characterised by accumulating disability over time.⁵

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:

The eligible population includes patients with clinical or radiological features suggestive of a relapsing or progressive inflammatory demyelinating disorder of the CNS, where multiple sclerosis (MS) is suspected and CSF evidence of intrathecal immunoglobulin synthesis may assist diagnosis. This may include patients presenting with CIS, optic neuritis, transverse myelitis, brainstem or cerebellar syndromes, progressive neurological symptoms suggestive of primary progressive MS, or MRI findings suspicious for inflammatory demyelination.¹

Patients suspected of having MS would typically be referred by a general practitioner, emergency physician, ophthalmologist or other medical practitioner to a neurologist for specialist assessment. The diagnostic work-up includes clinical examination, MRI of the brain and spinal cord, investigations to exclude alternative diagnoses, and lumbar puncture for CSF analysis where additional information is required.¹ CSF analysis is usually the final investigation prior to establishing a diagnosis, and is not required in all patients as a diagnosis of MS can be established by less invasive investigations such as MRI findings that corroborate clinical symptoms.¹

The proposed intervention is not intended for routine monitoring of established MS, disease activity or treatment response. It is limited to patients in whom MS remains under diagnostic assessment and where evidence of intrathecal immunoglobulin synthesis may clarify the diagnosis and inform subsequent management decisions.

Provide a rationale for the specifics of the eligible population:

The specifics of the eligible population are informed by the 2024 McDonald diagnostic criteria—an internationally recognised diagnostic framework for relapsing and progressive presentations of MS. Central to the criteria are the concepts of dissemination in space (DIS) and dissemination in time (DIT), in the absence of a better alternative diagnosis:¹

- **Dissemination in space (DIS)** refers to evidence of inflammatory demyelinating lesions affecting distinct CNS anatomical regions. The 2024 criteria add the optic nerve as a fifth anatomical location for demonstrating dissemination in space, alongside other CNS regions used in previous versions of the criteria.
- **Dissemination in time (DIT)** refers to evidence that inflammatory demyelinating disease has occurred at different points in time, which may be demonstrated clinically, radiologically, or through accepted paraclinical evidence as a substitute for DIT in specific situations.

Not all patients suspected of having MS will require laboratory confirmation of intrathecal immunoglobulin synthesis. Where clinical and MRI findings are sufficient to satisfy the McDonald diagnostic criteria and alternative diagnoses have been excluded, CSF testing may not be necessary.¹ A summary of the circumstances in which CSF testing may be used are summarised in **Table 1**.¹

Table 1 Clinical situations in which CSF testing is indicated based on the 2024 McDonald diagnostic criteria for MS

Clinical situation	Minimum diagnostic logic	CSF testing indicated?	Implication for kFLC / OCB testing
Typical clinical attack or progressive presentation + lesions in ≥ 4 of 5 typical CNS locations	MS can be diagnosed where there is strong spatial lesion burden across typical locations, after excluding a better alternative diagnosis. The five locations are periventricular, cortical/juxtacortical, infratentorial, spinal cord and optic nerve.	No	CSF kFLC/OCB is not required to establish a diagnosis if the clinical and MRI picture is otherwise sufficient.
Typical clinical attack or progressive presentation + DIS met, but DIT not demonstrated clinically or radiologically	DIS is present, but there is insufficient evidence that disease activity has occurred at different points in time.	Yes, as a substitute for DIT	Positive CSF (either CSF-restricted OCBs or elevated kFLC index) can demonstrate intrathecal immunoglobulin synthesis and support diagnosis.
Typical clinical attack or progressive presentation + limited lesion distribution	Lesions are suspicious for MS but do not clearly meet the full diagnostic threshold by MRI/clinical evidence alone.	Yes, if it helps resolve diagnostic uncertainty	CSF kFLC/OCB may provide supportive evidence, but cannot compensate for an overall presentation that is not sufficiently compatible with MS.

Clinical situation	Minimum diagnostic logic	CSF testing indicated?	Implication for kFLC / OCB testing
Progressive neurological presentation suspicious for primary progressive MS	The 2024 criteria use a unified diagnostic framework for relapsing and progressive MS, rather than a separate PPMS pathway.	Often yes	CSF testing may be important where clinical progression and MRI findings are suggestive but not independently conclusive.
Radiologically isolated syndrome or incidental MRI lesions suspicious for MS	The 2024 criteria allow diagnosis in some people before a typical clinical attack, but only where imaging/paraclinical evidence is sufficiently specific and alternative diagnoses are excluded.	Potentially yes	CSF kFLC/OCB may contribute supportive specificity, particularly as clinical symptoms are absent and misdiagnosis risk is higher.
Nonspecific symptoms without objective clinical or MRI evidence of demyelination	Symptoms alone do not establish a demyelinating syndrome or MS-compatible presentation.	No	CSF kFLC/OCB testing should not be used as a screening test for vague symptoms such as isolated fatigue, dizziness, pain, mood symptoms or cognitive complaints.
Atypical presentation or red flags suggesting another disorder	McDonald criteria require that there is no better alternative diagnosis.	No	CSF testing may be clinically useful for differential diagnosis, but kFLC/OCB should not be used to inform an MS diagnosis where infection, malignancy, vascular disease, MOGAD, NMOSD or another condition is more likely.
Established MS under monitoring or treatment follow-up	Diagnosis has already been made; the criteria are diagnostic, not monitoring criteria.	No	CSF kFLC/OCB testing is not intended for routine monitoring of disease activity, prognosis or treatment response.

Abbreviations: **CNS**=central nervous system, **CSF**=cerebrospinal fluid, **DIS**=dissemination in space, **DIT**=dissemination in time, **kFLC**=kappa free-light chain, **MOGAD**=myelin oligodendrocyte glycoprotein antibody-associated disease, **MRI**=magnetic resonance imaging, **MS**=multiple sclerosis, **NMOSD**=neuromyelitis optica spectrum disorder, **OCB**=oligoclonal band, **PPMS**=primary progressive multiple sclerosis.

Are there any prerequisite tests?

No

Owing to the invasiveness of CSF puncture, kFLC index and OCB testing are typically reserved following MRI results that indicate a possible demyelinating disorder (under MBS item 63125, 63049, and 63219); however, confirmed MRI suspicion of a demyelinating disorder is not a strict prerequisite test in the sense that it is not currently a mandated prerequisite for the comparator investigation of intrathecal Ig synthesis, OCB testing (MBS item 71062), rather that this testing cascade reflects good practice.

In the hospital setting, CSF testing for intrathecal synthesis may occur prior to MRI, in the acute setting, to exclude infection and to work up for a demyelinating or neuro-inflammatory condition.

Table 2 Imaging tests commonly conducted prior to OCB and kFLC index testing

Item 63125	Group I5 - Magnetic Resonance Imaging
MRI—scan of head and cervical spine (including MRA, if performed) for demyelinating disease of the central nervous system (R) (Contrast) Bulk bill incentive (Anaes.) Fee: \$566.90 Benefit: 75% = \$425.20 85% = \$481.90 (See para IN.0.19 of explanatory notes to this Category)	
Item 63049	Group I5 - Magnetic Resonance Imaging
MRI—scan of head (including MRA, if performed) for demyelinating disease of the brain (R) (Contrast) Bulk bill incentive (Anaes.) Fee: \$463.80 Benefit: 75% = \$347.85 85% = \$394.25 (See para IN.0.19 of explanatory notes to this Category)	
Item 63219	Group I5 - Magnetic Resonance Imaging
MRI—scan of 3 contiguous or 2 non contiguous regions of the spine for demyelinating disease (R) (Contrast) Bulk bill incentive (Anaes.) Fee: \$515.30 Benefit: 75% = \$386.50 85% = \$438.05 (See para IN.0.19 of explanatory notes to this Category)	

Are the prerequisite tests MBS funded?

N/A

Provide details to fund the prerequisite tests:

N/A

Intervention

Name of the proposed health technology:

The proposed intervention is kFLC index testing.

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

The kFLC index is calculated from paired measurements of kFLC in cerebrospinal fluid (CSF) and serum, combined with measurements of CSF and serum albumin. The index is calculated using the CSF/serum kFLC quotient divided by the CSF/serum albumin quotient, which provides evidence of intrathecal immunoglobulin synthesis while accounting for blood–CSF barrier function:^{6, 7}

$$kFLC\ index = \frac{Q_{kFLC}}{Q_{alb}} = \left[\frac{\frac{CSF\ kFLC\ (mg/L)}{Serum\ kFLC\ (mg/L)}}{\frac{CSF\ albumin\ (mg/L)}{Serum\ albumin\ (mg/L)}} \right]$$

CSF is collected via lumbar puncture, with a paired serum sample collected in the same diagnostic episode via venepuncture within an appropriate time window. Bayside Health (the Alfred), that conducts testing in Victoria, specify that paired serum should be collected within 24 hours of the CSF sample.⁸

Testing is performed using automated immunoassay platforms, including nephelometry or turbidimetry, that provide quantifiable and rater-independent results.^{6, 7} In Australian practice, Bayside Health (the Alfred) lists immunonephelometry as their method for kFLC index testing, and notes that OCB testing may be reflexed for samples where a kFLC index cannot be calculated.⁸ The kFLC index result is reported as a quantitative score; the Alfred notes a result ≥ 6.1 is consistent with intrathecal immunoglobulin synthesis.⁸

The treating neurologist would interpret the kFLC index result alongside the patient's clinical presentation, MRI findings and consideration of alternative diagnoses. A positive kFLC index may support an MS diagnosis under the 2024 McDonald criteria, while a negative or equivocal result does not exclude MS and may require further clinical review, interval imaging, or investigation for alternative diagnoses.¹

Identify how the proposed technology achieves the intended patient outcomes:

B cells and plasma cells play an important role in MS because they help sustain inflammation within the CNS. B cells can activate and coordinate other immune cells by presenting antigens and releasing inflammatory signals. In some patients, B cells and plasma cells also accumulate within the CNS and meninges, where they contribute to ongoing local immune activity. One result of this activity is the production of immunoglobulins within the CNS, known as intrathecal immunoglobulin synthesis.^{9, 10}

kFLCs are small protein fragments produced during immunoglobulin synthesis by activated plasma cells.⁹ When kFLC levels are elevated in CSF relative to serum and blood–CSF barrier function this can indicate intrathecal immunoglobulin synthesis. Intrathecal immunoglobulin synthesis reflects compartmentalised CNS plasma cell activity and is a recognised supportive feature of MS diagnosis, traditionally assessed using CSF-restricted oligoclonal IgG bands.^{10, 11} This is the biological basis for using CSF biomarkers such as OCB and kFLC index to support the diagnostic assessment of patients suspected of having MS.¹⁰

Accurate MS diagnosis supports timely counselling, specialist monitoring and initiation of disease-modifying therapy. It also reduces the risk of delayed treatment, unnecessary investigations, and inappropriate MS therapy in people with alternative diagnoses.⁹

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

No

The proposed health technology is kFLC index testing, not a specific proprietary assay, analyser platform or trademarked product. The service can be delivered using any suitably validated kFLC assay and laboratory method capable of measuring kFLC and albumin in paired CSF and serum samples and calculating/reporting a kFLC index.

Several commercial assay/platform combinations may be suitable, including assays from Siemens and The Binding Site, provided the laboratory has validated the method, applies appropriate quality assurance, and reports results using assay- and laboratory-validated thresholds. The proposed MBS item should therefore be technology- and manufacturer-neutral, rather than restricted to a particular branded reagent, analyser or trademarked test name.

Explain whether 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

Provide details and explain:

The proposed clinical service is intended to be claimed once per diagnostic episode. The proposed MBS item is not intended to be used for routine monitoring of established MS. OCB testing is intended to remain available for follow-up of a kFLC index result where the specialist considers it necessary, including equivocal (i.e. kFLC close to diagnostic threshold; faint or subtle OCB bands) or discordant presentations (i.e. CSF result conflicts with clinical and/or MRI findings),¹² or in the case where clinicians continue to request OCB as a suitable alternative to the kFLC index. This restriction reflects the McDonald criteria's requirement for expert clinical interpretation, and the consensus recommendation that kFLC index and OCB be interpreted in the context of clinical and MRI assessments.^{1, 6}

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

kFLC index testing will be provided by Approved Pathology Practitioners (APPs) in line with other services listed on the MBS Pathology Services Table.

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:

Referral for kFLC index testing should be limited to specialist consultant physicians involved in the diagnostic assessment of suspected MS. In the vast majority of cases this will be a treating neurologist, noting that a small proportion of requesting may come from other specialist physicians, for example emergency physicians, ophthalmologists, etc.

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:

Testing will be delivered only by APPs with appropriate scope of practice in NATA Accredited Pathology Laboratories on referral only by registered Medical Practitioners (non-pathologists) in line with other tests in the MBS Pathology Services Table.

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

- ☐ 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)

The proposed service is the laboratory measurement and reporting of the kFLC index. Specimen collection may occur in outpatient, inpatient or emergency settings, depending on the clinical presentation and local pathway. In acute or inpatient settings, lumbar puncture and CSF testing may be undertaken as part of broader assessment for infection, inflammatory demyelinating disease or other neurological conditions. In outpatient settings, testing may be arranged following specialist assessment and MRI where CSF evidence of intrathecal immunoglobulin synthesis is required.

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:

The appropriate comparator is OCB testing, delivered as part of the current diagnostic work-up for patients with suspected MS.¹

In the absence of MBS-funded kFLC index testing, patients requiring CSF evidence of intrathecal immunoglobulin synthesis would undergo OCB testing alongside clinical assessment by a neurologist, MRI of the brain and spinal cord, and investigations to exclude alternative diagnoses.

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

OCB testing is MBS-funded under item 71062, which covers electrophoresis, immunofixation, immunoelectrophoresis or isoelectric focusing of CSF for the detection of oligoclonal bands, including serum electrophoresis for comparison purposes where required.

Item 71062	Group P4 - Immunology
Electrophoresis and immunofixation or immunoelectrophoresis or isoelectric focussing of CSF for the detection of oligoclonal bands and including if required electrophoresis of the patient's serum for comparison purposes - 1 or more tests	
Fee: \$46.25 Benefit: 75% = \$34.70 85% = \$39.35	

Provide a rationale for why this is a comparator:

OCB testing is the appropriate comparator because it is the established CSF biomarker used to demonstrate intrathecal immunoglobulin synthesis in suspected MS. The revised 2024 McDonald criteria introduced CSF kFLC index testing as a biomarker that may be used as an alternative to OCB testing to demonstrate intrathecal immunoglobulin synthesis.¹ Concordance between kFLC index and OCB testing is high but not perfect, at approximately 90%; therefore, in a small proportion of cases a reflex follow-up test (i.e. OCB following kFLC, or vice versa) may be beneficial, particularly to confirm an equivocal result, or a CSF result that is discordant with the clinical and radiological assessments.^{1, 6, 13}

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?

- ☐ 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:

The proposed kFLC service is expected to partially substitute for OCB testing under MBS item 71062. In patients suspected of having MS who require evidence of intrathecal immunoglobulin synthesis, kFLC index testing is primarily intended to be used as an alternative CSF biomarker, noting that it may have clinical utility as a reflex test in certain circumstances.

OCB testing is expected to remain clinically relevant where the kFLC index cannot be calculated, where the result is equivocal or discordant with the clinical and MRI findings, or where the treating specialist has a strong preference for OCB testing. Similarly, kFLC testing may help clarify equivocal OCB results, noting that OCB testing is qualitative and subject to inter-reader variation.^{6, 7, 14}

The precise extent of substitution is uncertain and will depend on local laboratory availability, clinician preference, reflex-testing practices and the rate of equivocal or discordant results. However, the proposed service is expected to have a modest budget impact because it would largely replace, rather than add to, existing CSF biomarker testing for suspected MS.

Outcomes

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):

- ☒ 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:

The key outcome is accurate diagnostic classification in patients undergoing assessment for suspected MS. The kFLC index provides evidence of intrathecal immunoglobulin synthesis, which may contribute to satisfaction of the McDonald diagnostic criteria when interpreted with clinical findings, MRI and exclusion of alternative diagnoses. A positive result may increase diagnostic confidence and support subsequent counselling, monitoring and consideration of disease-modifying therapy where the overall criteria for MS are met.^{1, 6, 14}

Compared with OCB testing, the proposed service is not expected to materially change downstream clinical management where results are informative and concordant. Rather, kFLC is proposed as an alternative method for answering the same diagnostic question, with comparable diagnostic performance and practical laboratory advantages including quantitation, automation and reduced dependence on subjective visual interpretation.^{1, 6, 14}

In some patients, the test information may affect resource use by reducing the need for OCB testing, supporting faster reporting, or guiding reflex testing where the initial CSF biomarker result is equivocal, technically uninterpretable or discordant with the clinical and radiological assessment. A negative or equivocal kFLC result does not exclude MS and should prompt further clinical review, interval imaging, OCB testing or investigation of alternative diagnoses where clinically indicated.^{1, 14}

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):

kFLC testing is currently funded through limited local hospital or laboratory arrangements, or charged out-of-pocket as a non-MBS rebated service. Bayside Health (The Alfred) provides kFLC index testing for a private fee of \$60.⁸

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

MBS item number (where used as a template for the proposed item)	N/A
Category number	6
Category description	Pathology Services
Proposed item descriptor	Detection and quantitation of kappa free-light chains in cerebrospinal fluid and serum, detection and quantitation of albumin in cerebrospinal fluid and serum, and calculation and report of a kappa free light chain index for the diagnosis of multiple sclerosis, requested by a specialist consultant physician - once per diagnostic episode.
Proposed MBS fee	Fee: \$60.00 Benefit: 75% = \$45.00 TBD 85% = \$50.70
Indicate the overall cost per patient of providing the proposed health technology	\$60
Please specify any anticipated out of pocket expenses	\$0
Provide any further details and explain	Costing breakdown, see attached spreadsheet. Note, while this application proposes a separate service for kFLC, OCB testing will still be required in specific circumstances. It is not intended that OCB and kFLC both be used on the same patient as a point of standard practice. To avoid the risk of over-use, we propose wording be added to either the item descriptor or a practice note for item 71062, noting that OCB testing remain eligible when kFLC testing is "indeterminate or unable to be reported". Situations in which OCB might be tested include: 1 - insufficient sample volume 2 - borderline kFLC index 3 - unable to undertake kFLC testing 4 - kFLC result contradicts strong pre-test probability 5 - based on requesting clinician preference

	We seek the Department and Committees' advice on the most appropriate way to ensure the risk of over-use is minimised.
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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:

Before kFLC index testing is used, patients would undergo specialist assessment for suspected MS, including clinical history and neurological examination to determine whether the presentation is consistent with a typical demyelinating syndrome, progressive neurological presentation, or other MS-compatible presentation, and to assess for alternative diagnoses.¹

Patients would then usually undergo MRI of the brain and spinal cord, with further investigations as required to exclude mimics. Where the diagnosis remains uncertain and CSF evidence of intrathecal immunoglobulin synthesis would assist with the application of the McDonald criteria, CSF would be collected by lumbar puncture and a paired serum sample is collected in the same diagnostic episode.^{1, 6, 7}

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 material change is proposed to the pre-test clinical pathway, including the decision to undertake lumbar puncture. The proposed change is the laboratory biomarker used to assess intrathecal immunoglobulin synthesis, with kFLC index testing available as an alternative to OCB testing.^{1, 6}

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:

The proposed service is delivered in conjunction with the existing diagnostic pathway for suspected MS. Required resources include lumbar puncture to collect CSF, paired venepuncture for serum collection, specimen handling and transport to an accredited pathology laboratory, and laboratory measurement of kFLC and albumin in both CSF and serum.

The laboratory then calculates the kFLC index and issues a quantitative result with appropriate interpretive reporting. Testing is performed on automated immunoassay platforms, subject to local validation, assay-specific thresholds and quality-assurance processes. The result is then reviewed by the treating neurologist alongside the patient's clinical presentation, MRI findings and other investigations.^{6, 7}

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

The comparator service is delivered through the existing CSF testing pathway for suspected MS. Required resources include lumbar puncture to collect CSF, paired serum collection for comparison, specimen handling and transport to an accredited pathology laboratory, and laboratory testing for CSF oligoclonal bands using electrophoresis or isoelectric focusing with immunofixation or immunoblotting.

The laboratory issues an interpretive report indicating whether CSF-restricted oligoclonal bands are present. The result is then reviewed by the treating neurologist alongside the patient's clinical presentation, MRI findings and other investigations.⁶

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

The main difference is in the laboratory method. The kFLC index is a quantitative assay that measures kFLC and albumin in paired CSF and serum samples, calculates an index, can be performed on automated immunoassay platforms subject to local validation, and has higher reagent costs. In contrast, OCB testing is a qualitative method using electrophoresis or isoelectric focusing with immunofixation or immunoblotting, and requires manual interpretation by a senior scientist or pathologist. Both pathways require the same pre-analytical resources, including lumbar puncture, specimen handling, paired serum collection, and neurology review.⁷

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:

After kFLC index testing, the result is reviewed by the treating neurologist in the context of the patient's clinical presentation, MRI findings and exclusion of alternative diagnoses.

A positive kFLC index provides evidence of intrathecal immunoglobulin synthesis. Where the overall clinical, radiological and laboratory findings satisfy the McDonald criteria, MS may be diagnosed and the patient managed according to standard clinical practice, including counselling, monitoring and initiation of disease-modifying therapy.^{1, 5}

A negative or equivocal kFLC index does not exclude MS. If clinical suspicion remains, the patient may require further diagnostic evaluation, interval clinical or MRI follow-up, OCB testing, or other investigations to assess alternative diagnoses.^{1, 6}

Where the kFLC result is discordant with the clinical or MRI findings, or the presentation is atypical, further assessment is required before confirming MS. This may include OCB reflex testing, additional CSF studies, serological testing, repeat or extended imaging, neurophysiology, or other investigations guided by the differential diagnosis.^{1, 6}

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

Same as above.

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

Downstream management is expected to be the same following an informative positive kFLC index or positive OCB result. In both pathways, the treating neurologist interprets the result alongside clinical features, MRI findings and exclusion of alternative diagnoses, and manages the patient according to standard MS diagnostic and treatment pathways where the criteria are fulfilled. The main difference is likely to arise in equivocal or discordant cases. A non-informative, borderline or clinically inconsistent kFLC result may lead to OCB testing or further diagnostic investigations, while an equivocal OCB result may similarly prompt kFLC testing or additional review. The proposed claim is therefore one of non-inferior diagnostic performance and potential laboratory practicality, rather than superior long-term patient health outcomes.^{1, 6, 14}

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

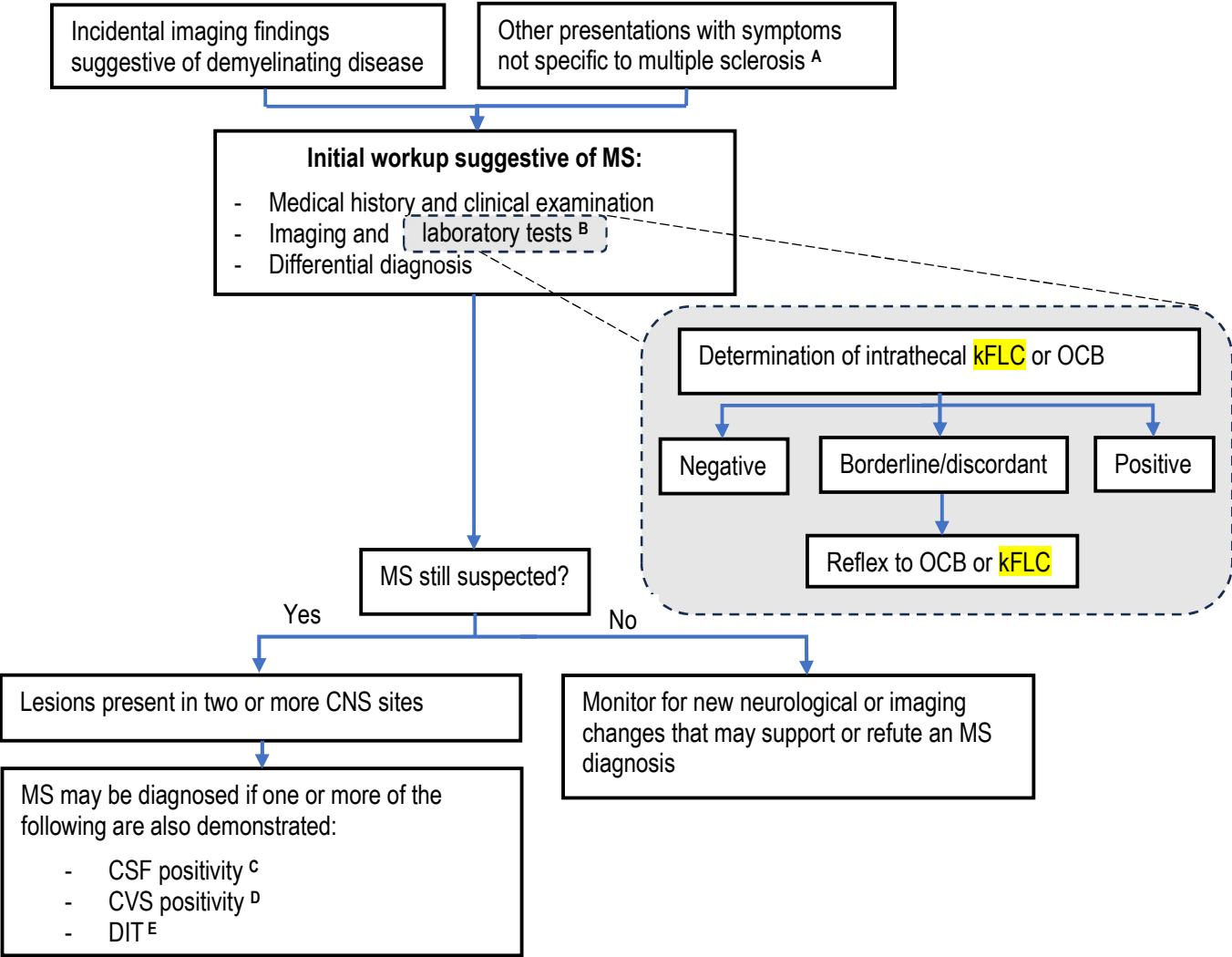


Figure 1 Clinical management algorithm indicating the use of kFLC index testing as an alternative to OCB testing for patients suspected of having MS

Source: Adapted from Hegen et al 2023⁶ and Montalban et al 2025¹

Abbreviations: **CNS**=central nervous system, **CSF**=cerebrospinal fluid, **CVS**=central vein sign, **DIT**=dissemination in time, **MS**=multiple sclerosis.

Notes:

- ^A Presentations might include: (1) symptoms or signs overlapping those of MS but with no characteristic attack; or (2) paroxysmal symptoms (e.g. trigeminal neuralgia), seizures, and other symptoms.
- ^B This pop-out box with a grey background demonstrates the flowchart for CSF testing. Note, as the diagnosis of MS is dependent on a number of factors (including DIT, DIS, CSF positivity, and/or CVS positivity), a comprehensive stepwise flowchart differentiating these not been presented.
- ^C CSF positivity is demonstrated by presence of OCB or kFLC.
- ^D In patients with typical clinical presentations and typical lesions in one region, the presence of the select 6 CVS plus dissemination in time or positive CSF is sufficient for diagnosis
- ^E DIT is demonstrated by the presence of one or more new T2 lesions or one or more gadolinium-positive lesions or a clinical attack.

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)?

- ☐ Superior
- ☒ Non-inferior
- ☐ Inferior

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

The overall claim is that kFLC index testing has non-inferior safety and diagnostic performance compared with OCB testing for demonstrating intrathecal immunoglobulin synthesis in patients being assessed for suspected MS.^{1, 6, 14}

This claim is supported by evidence that kFLC index testing has similar diagnostic accuracy to OCB testing for MS and clinically isolated syndrome, and by its recognition in the 2024 McDonald criteria as an alternative marker of CSF positivity. Both tests address the same diagnostic question and are used for the same purpose within the clinical pathway, alongside neurological assessment, MRI and exclusion of alternative diagnoses.^{1, 6, 7, 14}

The proposed claim is not that kFLC testing improves long-term health outcomes compared with OCB testing, but that it provides a clinically acceptable alternative method for assessing intrathecal immunoglobulin synthesis, with potential practical laboratory advantages as a quantitative and automatable assay.

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

A requestor would seek to use kFLC index testing because it provides a quantitative and more readily automated measure of intrathecal immunoglobulin synthesis, and is recognised in the 2024 McDonald criteria as an alternative to OCB testing for CSF positivity in suspected MS.¹

Compared with OCB testing, kFLC index testing may offer practical laboratory advantages, including reduced manual interpretation, less inter-reader variability, faster reporting and broader implementation on automated immunoassay platforms.^{1, 6, 7} These may improve access to CSF biomarker testing where OCB testing is delayed, difficult to interpret, or requires referral to another laboratory.

Identify how the proposed technology achieves the intended patient outcomes:

See previous response.

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

A change in clinical management? No

A change in health outcome? No

Other benefits? Yes

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

kFLC index testing may provide practical benefits over OCB testing because it is quantitative, more readily automated and less dependent on subjective visual interpretation. This may improve reproducibility, support more consistent reporting, and reduce laboratory handling time.^{6, 7}

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?

- ☒ More costly
☐ Same cost
☐ Less costly

Provide a brief rationale for the claim:

The proposed service for kFLC index testing is claimed to be more costly than the comparator on an immediate test-cost basis, but with a modest expected budget impact as it is proposed as a direct alternative to OCB testing for most patients.

Costing estimates for kFLC index testing are \$51.42 per patient at the 85% rebate, comprising \$44.50 in consumables and \$6.92 in labour. The corresponding estimated cost for paired CSF/serum OCB testing is \$43.34 per patient. Using the current 85% MBS benefit for OCB testing under item 71062 (\$39.35) and a provisional kFLC benefit of \$51.00 based on a \$60 fee, the incremental benefit is \$11.65 per service.

Based on average utilisation of item 71062 between 2023–2025 (2,500 services per year), the estimated additional cost to the health system would be approximately \$29,125 per year, assuming complete substitution. As an upper estimate, using average utilisation from 2018–2025 (3,500 services per year), the additional cost would be approximately \$40,775 per year. These estimates assume no increase in total CSF biomarker testing and are sensitive to the extent of add-on or reflex testing.

Note, these estimates have assumed bulk-billing for item 71062, the cost of which is substantially driven by staffing costs owing the qualitative nature of the test. Consultation feedback from labs that conduct OCB testing suggests that the true cost of providing this service is significantly higher than the MBS rebate, with the additional cost above the rebate typically absorbed by labs. Estimates of the true cost of OCB testing, depending on the lab, range between \$43.34 and \$88.90. Therefore, while it can be expected that an item for kFLC index testing will result in a net cost to the MBS based on the current rebate for item 71062, in real terms it is expected to result in a net cost saving to health system more broadly.

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',

#	Study, design	Title of journal article or research project	Short description of research	Link
1	Montalban, et al. 2025 ¹ Clinical practice guideline	Diagnosis of multiple sclerosis: 2024 revisions of the McDonald criteria	The 2024 McDonald criteria recognise CSF kFLC assessment as an alternative to oligoclonal bands for demonstrating intrathecal immunoglobulin synthesis. This expands diagnostic options, potentially improving access through a quantitative, automatable biomarker, while retaining MRI and clinical assessment to avoid misdiagnosis.	PMID 41005340
2	Hegen, et al. 2023 ¹⁴ Systematic review and meta-analysis	Cerebrospinal fluid kappa free light chains for the diagnosis of multiple sclerosis: A systematic review and meta-analysis	This systematic review and meta-analysis of 32 studies for kFLC index (3,322 CIS/MS patients and 5,849 controls) found CSF kFLC measures, particularly the kappa index, have high diagnostic accuracy for multiple sclerosis and broadly comparable performance to oligoclonal bands. kFLC testing offers a quantitative, automated and potentially faster alternative, although optimal cut-offs varied across studies and require local laboratory validation.	PMID 36453167
3	Levrut, et al. 2023 ¹⁵ Study of diagnostic accuracy	Kappa Free Light Chain Biomarkers Are Efficient for the Diagnosis of Multiple Sclerosis	This multicentre study found CSF kFLC biomarkers, especially the kappa index, performed comparably with oligoclonal bands for diagnosing multiple sclerosis. kFLC testing showed high sensitivity and specificity, supported earlier diagnostic classification, and offers a rapid, quantitative and automatable alternative to labour-intensive oligoclonal band analysis.	PMID 36376096

#	Study, design	Title of journal article or research project	Short description of research	Link
4	Hegen, et al. 2023 ¹⁶ Consensus statement	Cerebrospinal fluid kappa free light chains for the diagnosis of multiple sclerosis: A consensus statement	This consensus statement supports CSF kFLC testing, particularly the kappa index, as a reliable marker of intrathecal immunoglobulin synthesis in suspected multiple sclerosis. It recommends locally validated cut-offs and quality-assured methods, noting kFLC is quantitative, automatable and diagnostically comparable with OCB testing.	PMID 36527368
5	Moreno-Navarro, et al. 2025 ¹⁷ Retrospective cohort	Kappa free light chain index as a diagnostic and prognostic biomarker in multiple sclerosis	This retrospective cohort study found kFLC index had diagnostic performance comparable to OCB in adults with a first demyelinating episode, using both 2017 and proposed 2024 McDonald criteria. kFLC index ≥ 100 was also associated with short-term infratentorial or spinal-cord lesion accrual, but requires validation.	PMID 40986067
6	Dekeyser, et al. 2024 ⁷ Study of diagnostic accuracy	Inter-assay diagnostic accuracy of cerebrospinal fluid kappa free light chains for the diagnosis of multiple sclerosis	This inter-assay study found kFLC index and klgG index had strong diagnostic accuracy for MS, outperforming oligoclonal bands in AUC. However, optimal cut-offs differed between assay platforms, reinforcing that kFLC implementation requires assay-specific validation rather than assuming a universal threshold.	PMID 38745673

Abbreviations: **AUC**=area under the curve, **CIS**=clinically isolated syndrome, **CSF**=cerebrospinal fluid, **kFLC**=kappa free-light chain, **klgG**=kappa immunoglobulin G, **MRI**=magnetic resonance imaging, **MS**=multiple sclerosis, **OCB**=oligoclonal band

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

#	Study design	Title of journal article or research project	Short description of research	Date Link
1	Prospective, multicentre, cohort study	Kappa Free Light Chains (kFLC) in Multiple Sclerosis (MS) and Clinically Isolated Syndrome (CIS) (PRO-kFLC) NCT07183020	This observational multicentre study will compare CSF kFLC with oligoclonal bands in 1,142 adults with MS or CIS. It aims to determine whether kFLC is superior, inferior or equivalent for CSF diagnostic work-up, while addressing implementation uncertainties around standardised cut-offs and longitudinal prediction of CIS conversion.	Estimated completion December 2026 NCT07183020

Abbreviations: **CIS**=clinically isolated syndrome, **CSF**=cerebrospinal fluid, **kFLC**=kappa free-light chain, **MS**=multiple sclerosis.

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