

MSAC application 1831

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

Application for MBS eligible service or health technology

HPP Application number:

HPP200431

Application title:

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

Submitting organisation:

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA

Submitting organisation ABN:

52000173231

Application description

Succinct description of the medical condition/s:

Multiple sclerosis is a chronic, neurodegenerative condition in which the immune system mistakenly attacks the protective covering of nerves in the brain and spinal cord, called myelin. This damage to the nerves, or demyelination, disrupts communication between the brain and the rest of the body and can cause a wide range of symptoms, including vision problems, numbness, weakness, fatigue, poor balance, difficulties with walking, and changes in memory or concentration. Accurate diagnosis informs the appropriate use of disease-modifying therapies that are intended to slow the accumulation of disability associated with demyelination.

Succinct description of the service or health technology:

Kappa free-light chains are small protein fragments, produced by antibody-forming immune cells, that are released during immunoglobulin production. The kFLC index compares kFLC concentrations in cerebrospinal fluid and serum, while using albumin to correct for the normal transfer of proteins from the blood into cerebrospinal fluid. Because albumin is produced outside the central nervous system, the cerebrospinal fluid-to-serum albumin ratio provides a measure of blood–cerebrospinal fluid barrier permeability. An elevated kFLC index indicates that the amount of kFLC in cerebrospinal fluid is greater than would be expected from passive transfer alone, supporting local antibody production within the central nervous system, which is a marker of MS disease activity.

Application contact details

Are you the applicant, or are you a consultant or lobbyist acting on behalf of the applicant?

Applicant

Are you applying on behalf of an organisation, or as an individual?

Organisation

Applicant organisation name:

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA

Application details

Does the implementation of your service or health technology rely on a new listing on the Pharmaceutical Benefits Scheme (PBS) and/or the Prescribed List?

No

Is the application for a new service or health technology, or an amendment to an existing listed service or health technology?

New

What is the type of service or health technology?

Investigative

Please select the type of investigative health technology:

Immunology

PICO sets

Application PICO sets:

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

State the purpose(s) of the health technology for this PICO set and provide a rationale:

Purpose category:

Diagnosis / sub-classification

Purpose description:

To establish a diagnosis or disease (sub)classification in symptomatic or affected patients

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.

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. 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. 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.

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.

Select the most applicable Medical condition terminology (SNOMED CT):

Multiple sclerosis

Intervention

Name of the proposed health technology:

Kappa free-light chain index testing

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 health care system). This includes identifying health care resources that are needed to be delivered at the same time as the comparator service:

The comparator is oligoclonal band (OCB) testing, delivered as part of the current diagnostic work-up for patients with suspected MS. 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.

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. 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.

Outcomes

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

Due to the positioning of kFLC index testing as an alternative to OCD testing, 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.

Compared with OCB testing, the proposed service is not expected to materially change downstream clinical management where results are informative and concordant with clinical and MRI assessments.

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.

Proposed MBS items

Please provide at least one proposed item with their descriptor and associated costs, for each population / intervention:

Proposed item:

AAAAA

Category number:

6 - Pathology Services

Category description:

4 - Immunology

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:

\$60.00

Indicate the overall cost per patient of providing the proposed health technology:

\$60.00

Please specify any anticipated out of pocket expenses:

\$0.00

Provide any further details and explain:

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

How is the technology / service funded at present? (For example: 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.

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)?

Non-inferior

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

Compared to OCB testing (item 71062), KFLC is claimed to have non-inferior effectiveness and safety.

Estimated utilisation

Estimate the prevalence and/or incidence of the proposed population:

The proposed population includes patients undergoing diagnostic assessment for suspected MS, rather than all people living with established MS. In this context, prevalence data is not relevant to the estimated utilisation of the proposed service. Per the McDonald diagnostic framework, fulfilment of dissemination in space (DIS) and dissemination in time (DIT) are sufficient to diagnose MS in certain circumstances. Therefore, not all patients suspected of MS will require laboratory confirmation via OCB or kFLC index testing. Given the recommendation in the McDonald criteria that kFLC is a suitable alternative to OCB testing, the best estimate for the size of the total eligible population is therefore not disease incidence, but rather the utilisation of OCB testing per MBS item 71062 (see Table A1 in the attachment).

Provide the percentage uptake of the proposed health technology by the proposed population:

Year 1 estimated uptake (%):

40

Year 2 estimated uptake (%):

50

Year 3 estimated uptake (%):

60

Year 4 estimated uptake (%):

70

Estimate the number of patients who will utilise the proposed technology for the first full year:

1,064

Optionally, provide details:

The total number of patients estimated to uptake the service in the first full year has been calculated as 40% of the average number of services for MBS item 71062

claimed over the past four years (approximately 2660 services/yr). kFLC index testing is currently limited to several laboratories in Australia due to the lack of MBS funding. It is expected that uptake will increase following the creation of an MBS item for kFLC index testing, noting that the speed of uptake, and relative replacement of OCB testing, is difficult to estimate. Testing will be required once per diagnostic episode, as the item is not intended for monitoring disease progression or treatment response.

Will the technology be needed more than once per patient?

No, once only

Consultation

List all entities that are relevant to the proposed service / health technology. The list can include professional bodies / organisations who provide, request, may be impacted by the service/health technology; sponsor(s) and / or manufacturer(s) who produce similar products; patient and consumer advocacy organisations or individuals relevant to the proposed service/health technology.

Entities who provide the health technology/service:

PATHOLOGY AUSTRALIA LIMITED

PUBLIC PATHOLOGY AUSTRALIA

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA

AUSTRALASIAN ASSOCIATION FOR CLINICAL BIOCHEMISTRY AND LABORATORY MEDICINE LIMITED

AUSTRALASIAN SOCIETY OF CLINICAL IMMUNOLOGY AND ALLERGY LIMITED

Entity who requests the health technology/service:

AUSTRALIAN AND NEW ZEALAND ASSOCIATION OF NEUROLOGISTS

Entities who may be impacted by the health technology/service:

THE ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

AUSTRALIAN SOCIETY OF OPHTHALMOLOGISTS LIMITED

THE AUSTRALASIAN COLLEGE FOR EMERGENCY MEDICINE

Patient and consumer advocacy organisations relevant to the proposed service/health technology:

MULTIPLE SCLEROSIS AUSTRALIA

MULTIPLE SCLEROSIS QUEENSLAND LTD
THE MULTIPLE SCLEROSIS SOCIETY OF SOUTH AUSTRALIA & NORTHERN TERRITORY
INC
MSWA LIMITED
MS PLUS LTD
MS NURSES AUSTRALIA INC.

Entities who produce similar products:

THE BINDING SITE PTY LIMITED
SIEMENS HEALTHCARE PTY LTD

Regulatory information

Would the proposed health technology involve the use of a medical device, in-vitro diagnostic test, radioactive tracer or any other type of therapeutic good?

Yes

Has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

Yes

Is the therapeutic good classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

No

Please enter all relevant ARTG IDs:

ARTG ID	ARTG name
202167	Clinical chemistry-specific protein IVDs
179722	Clinical chemistry autoimmune IVDs

Is the intended purpose in this application the same as the intended purpose of the ARTG listing(s)?

Yes