MSAC Application 1769

Human leukocyte antigen testing for sensitivity to carbamazepine in patients with epilepsy

Application for MBS eligible service or health technology

MSAC Application Number:
1769

Application title:
Human leukocyte antigen (HLA) testing for sensitivity to carbamazepine in patients with epilepsy

Submitting organisation:
THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA

Submitting organisation ABN:
52000173231

Application description

Succinct description of the medical condition/s:
Carbamazepine is an anticonvulsant medication used in the first-line treatment of epilepsy and neuropathic pain. Although associated with milder side effects such as dizziness, drowsiness, ataxia, nausea, and vomiting, carbamazepine comes with a black box warning for severe dermatologic hypersensitivity reactions, specifically and more commonly, Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), as well as drug reaction with eosinophilia and systemic symptoms (DRESS), and maculopapular exanthema (MPE) involving the skin and mucous membranes (Phillips et al 2017). These potentially lethal adverse drug reactions typically occur within the first 3-months of commencing treatment with carbamazepine (Ahmed et al 2021; Karnes et al 2019; Maan et al 2023). Hypersensitivity to carbamazepine is an example of an immune-mediated adverse event that is associated with variants in the human leukocyte antigen genes (HLA-A and HLA-B) (Duong et al 2017; Pirmohamed 2023).

Succinct description of the service or health technology:
Targeted genotyping using real-time PCR of all individuals about to commence treatment with carbamazepine to identify HLA-A and HLA-B alleles (HLA-A*31:01 and HLA-B*15:02), that would place them at risk of developing SJS, TEN, DRESS or MPE. Genotyping results are presented as "positive" if one or two copies of the variant allele are present, that is, being heterozygous or homozygous for either the HLA-A*31:01 or HLA-B*15:02 alleles (Pirmohamed 2023).

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

Is the applicant organisation the organisation you are representing in the HPP today?
Yes

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

Please select any relevant MBS items.
-

What is the type of service or health technology?
Investigative

Please select the type of investigative health technology:
Molecular diagnostic tests

Please select the type of molecular diagnostics health technology:
Single variant assay

PICO Set

HLA sensitivity to carbamazepine

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

Purpose category:
Predisposition

Purpose description:
To identify a hereditary predisposition to disease(s) or condition(s) in affected or at risk but currently unaffected patients

Population

Describe the population in which the proposed health technology is intended to be used:
Carbamazepine is an anticonvulsant medication used in the first-line treatment of epilepsy, neuropathic pain stemming from trigeminal neuralgia, and acute manic and mixed episodes in bipolar I disorder.

Search and select the most applicable medical condition terminology (SNOMED CT):
Epilepsy

Intervention

Name of the proposed health technology:
HLA-A*31:01 and HLA-B*15:02 genotyping to predict hypersensitivity to carbamazepine

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:
As there is no other means of identifying patients carrying either the HLA-B*15:02 or HLA-A*31:01 allele, the nominated comparator is therefore no genotyping.

Outcomes

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

Adverse events (or avoidance of AE) from treatment i.e. avoidance of Stevens–Johnson syndrome, toxic epidermal necrolysis and drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome

Adverse events (or avoidance of AE) from change in patient management (treatment modifications)

Clinical Effectiveness Outcomes:

Direct evidence:

Change in patient health outcomes: mortality, morbidity, quality of life - comparing patients who receive genotype-guided therapy to those who receive carbamazepine.

Indirect evidence

Clinical utility: change in patient management/treatment resulting in change in patient outcomes: mortality, morbidity, quality of life

Health system resources:

Cost of HLA-B*15:02 and HLA-A*31:01 genotyping

Cost of toxicity-related hospitalisation, morbidity, mortality

Cost per quality-adjusted life years

Total Australian Government healthcare costs

As described in Figure 4, all patients prescribed carbamazepine for the control of neurological symptoms associated with epilepsy or trigeminal neuralgia or for neuropathic pain or mood disorders should undergo HLA-B*15:02 and HLA-A*31:01 genotyping prior to the commencement of therapy. Patients found to be heterozygous or homozygous for either allele should not commence treatment with carbamazepine but should be treated with an alternative anti-epileptic drug such as gabapentin.

Proposed MBS items

Proposed Item AAAAA

MBS item number:
-

Proposed category:
PATHOLOGY SERVICES

Proposed group:
GENETICS

Proposed item descriptor:
Genotyping of a patient for HLA-B*15:02 and HLA-A*31:01 variants prior to the initiation of treatment with the anticonvulsant drug and analgesic drug, carbamazepine, requested by a specialist or consultant physician.

Once per lifetime

Fee: $188 Benefit: 85% = $160

Proposed MBS fee:
$188.00

Indicate the overall cost per patient of providing the proposed health technology:
$188.00

Please specify any anticipated out of pocket costs:
$0.00

Provide details and explain:
Nil

How is the technology/service funded at present? (For example: research funding; State-based funding; self-funded by patients; no funding or payments):
Self-funded, state-based funding (minimal) – no public funding

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

Please state what the overall claim is, and provide a rationale:
Anticonvulsant medication is used as a first-line treatment option for the neurological symptoms of epilepsy and neuropathic pain. One of the more common and effective anti-epileptic drugs is carbamazepine. Although extremely rare, hypersensitivity reactions to carbamazepine can result in Stevens–Johnson syndrome, toxic epidermal necrolysis or drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome, all of which are associated with significant morbidity or mortality in individuals who are heterozygous or homozygous for HLA-A*31:01 or HLA-B*15:02 alleles. Genotyping before commencing therapy with carbamazepine can identify patients who are at high risk of toxicity, allowing treatment with an alternative drug for the indication. Pre-treatment genotyping is safe, has been demonstrated to reduce patient morbidity, mortality and hospitalisations.

Estimated utilisation

Estimate the prevalence and/or incidence of the proposed population:
For the purposes of HLA genotyping prior to patients commencing treatment with carbamazepine, it is important to estimate the incidence of epilepsy. As there is a lack of Australian data on the incidence of epilepsy, international estimates must be relied on. The systematic review and meta-analysis of international studies by Fiest et al (2017) estimates the incidence of epilepsy as 61.44 per 100,000 person-years (95% CI 50.75–74.38) (Fiest et al 2017). With Australia's current population of approximately 26.5 million people, this would translate to 16,282 incident epilepsy cases per year.

There is a paucity of data describing the incidence of trigeminal neuralgia in Australia, and again international estimates must be relied upon. Trigeminal neuralgia is a rare condition, with a systematic review reporting an annual incidence ranging from 4.3 to 8 per 100,000, with incidence increasing with age. Based on the current Australian population this would translate to incident trigeminal neuralgia cases per year ranging from 1,140 to 2,120.

Not all incident epilepsy or trigeminal neuralgia cases would be prescribed carbamazepine.

In addition, data describing the incidence of patients with neuropathic pain who would be prescribed carbamazepine is difficult to obtain as neoplastic, neuropathic and nociceptive pain are all classified as chronic pain.

Providing a percentage estimate of uptake is not really very helpful. As per the 'old' application, giving an estimated number of patients is far more useful.

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

Year 1 estimated uptake (%):
100

Year 2 estimated uptake (%):
100

Year 3 estimated uptake (%):
100

Year 3 estimated uptake (%):
100

Estimate the number of patients who will utilise the proposed technology for the first full year:
See attached table for estimated usage - Total – lower limit = 2,906, Total upper limit = 19,322

Optionally, provide details:
Based on international data, the number of incident epilepsy cases per year would be approximately 16,282, and the number of incident trigeminal neuralgia would range from 1,140 to 2,120. It should be noted that not all incident cases will be prescribed carbamazepine, therefore the figures in the table below would represent an over estimation of the number of patients likely to require genotyping. Based on Figure 1, approximately only 10% of epileptics would be prescribed carbamazepine (lower limit). In addition, there is a paucity of data reporting the trend of these conditions over time, therefore a 5% increase in the incident population per year has been factored in.

Will the technology be needed more than once per patient?
No, once only

Consultation

List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the health technology/service:

- Pathology Australia
- Public Pathology Australia
- The Royal College of Pathologists of Australasia (RCPA) - the applicant

List all appropriate professional bodies / organisations representing the group(s) of health professionals who request the health technology/service:

- Australasian College of Dermatologists
- Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists
- Australia and New Zealand Association of Neurologists
- Australia and New Zealand Child Neurology Society
- Epilepsy Society of Australia (ESA)
- Pharmaceutical Society of Australia
- Society of Hospital Pharmacists of Australia

List all appropriate professional bodies / organisations representing the group(s) of health professionals that may be impacted by the health technology/service:
N/A

List the patient and consumer advocacy organisations or individuals relevant to the proposed health technology:

- Epilepsy Action Australia
- Epilepsy Australia
- The Epilepsy Centre
- Trigeminal Neuralgia Association Australia

List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed service or health technology:
N/A

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)?
No

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?
Class III

Is the therapeutic good to be used in the service exempt from the regulatory requirements of the Therapeutic Goods Act 1989?
No

Is the therapeutic good classified by the TGA as for Research Use Only (RUO)?
No