MSAC application 1821

Testing for Chromogranin A in patients with neuroendocrine neoplasms

Application for MBS eligible service or health technology

HPP Application number:

HPP200375

Application title:

Chromogranin A (CgA) for monitoring well differentiated neuroendocrine neoplasms (NENs)

Submitting organisation:

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA

Submitting organisation ABN:

52000173231

Application description

Succinct description of the medical condition/s:

Metastatic neuroendocrine tumours (NETs) are cancers that arise from neuroendocrine cells found throughout the body, most commonly in the gastrointestinal tract, pancreas, and lungs. In metastatic disease, the cancer has spread beyond its original site and usually requires long-term monitoring to assess whether it is stable or progressing, and whether treatment remains effective.

Succinct description of the service or health technology:

Chromogranin A (CgA) testing is a laboratory blood test used to help monitor patients with metastatic NETs over time. It is used in addition to imaging, clinical assessment, and other investigations, and provides a relatively simple and minimally invasive way to detect changes that may indicate disease progression or response to treatment. This can help clinicians decide when closer review, further imaging, or a change in management may be needed.

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:
Clinical biochemistry

PICO sets

Application PICO sets:

PICO set name
Chromogranin A (CgA) for monitoring well differentiated neuroendocrine neoplasms (NENs)

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

Purpose category:

Monitoring

Purpose description:

To monitor a condition over time.

Purpose category:

Outcome / response assessment

Purpose description:

To assess an outcome or response following an intervention or treatment

Population

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

The proposed health technology (serum chromogranin A [CgA] monitoring) is intended for patients with confirmed neuroendocrine tumours (NETs) who have advanced/metastatic disease and are undergoing ongoing surveillance during treatment or active follow-up, where there is a clinical need to monitor for disease progression or recurrence. The technology is primarily intended for patients in whom CgA is clinically "trackable" (i.e., elevated at baseline and/or previously shown to correlate with tumour activity for that individual) so that serial measurements can be interpreted as a longitudinal marker of progression.
NETs are a subset of a broader category of neuroendocrine neoplasms (NEN)–a heterogeneous group with varying prognoses. These include well-differentiated NETs (graded G1–G3 by proliferation) and poorly differentiated neuroendocrine carcinomas (NECs) (high-grade, biologically aggressive). They most commonly arise in gastro-entero-pancreatic (GEP) sites (small intestine, rectum, pancreas) and lung, and may be described clinically as functional (hormone-secreting) vs non-functional.

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

Malignant neuroendocrine tumour

Intervention

Name of the proposed health technology:

Chromogranin A (CgA) 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:

For the proposed population, the appropriate comparator is current practice without serial CgA monitoring ("no CgA monitoring"), in which disease status is assessed using clinical review plus scheduled imaging, with selective use of other biochemistry depending on tumour functionality and symptoms.
In routine Australian practice, metastatic NET follow-up relies on regular clinician visits (usually specialist-led) for symptom review, treatment toxicity assessment, and physical examination, combined with planned cross-sectional imaging, typically CT or MRI at defined intervals (often ~3–12 monthly depending on grade, site, burden and treatment), to assess stability versus progression. When CT/MRI is equivocal, when there is clinical suspicion of progression, or when results are likely to alter management, patients may undergo somatostatin-receptor imaging (e.g. 68Ga DOTA-peptide PET/CT) and, in selected higher-grade cases, 18F-FDG PET.
While imperfect, CgA remains the most accessible and widely used biochemical marker for NETs, superior in performance to alternatives like pancreastatin or neuron-specific enolase, which are either less validated or less available in Australia. These additional markers are not commonly used in practice in Australia, and are therefore not considered to be relevant comparator tests to CgA testing.

Outcomes

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

CgA is a valuable biomarker for predicting relapse and assessing prognosis in patients with metastatic NENs, as it correlates with tumour burden, stage, and treatment response. The predictive and prognostic value of CgA for monitoring treatment response and relapse in patients with NENs is well-supported by clinical evidence.

CgA levels are useful for early detection of recurrence post-treatment. In patients with completely resected disease, an increase in CgA levels can precede clinical and

radiological evidence of relapse by several months. For instance, an increase in CgA values can anticipate clinical and objective disease recurrence after a period of 9-12 months. Additionally, a ≥40% increase in CgA levels during follow-up is associated with a higher probability of tumour progression or recurrence.

Baseline CgA levels correlate with tumour burden, stage, and grade, making it a valuable prognostic marker. Higher baseline CgA levels are associated with more advanced disease stages and poorer overall survival (OS). For example, patients with higher baseline CgA levels had significantly worse OS after adjusting for other factors. Furthermore, a decrease in CgA levels post-treatment is positively correlated with improved survival rates.

Serial measurements of CgA can help assess treatment efficacy and disease progression. Changes in CgA levels, such as normalisation or a ≥30% decrease, suggest a positive therapeutic response. Conversely, patients with serum CgA levels higher than 95 ng/mL have significantly shorter survival compared to those with lower levels.

Proposed MBS items

Proposed item: AAAAA

Category number:
P2

Category description:
Chemical

Proposed item descriptor:
Quantitation of chromogranin A (CgA) for a patient with a diagnosed neuroendocrine tumour, performed to establish a baseline and for serial monitoring of disease activity, to assist in identifying relapse/progression and in assessing response to treatment, where the patient has known metastatic disease, and the service is requested by a specialist or consultant physician.
Maximum 4 tests per year.

Proposed MBS fee:
$65.00

Indicate the overall cost per patient of providing the proposed health technology:
$65.00

Please specify any anticipated out of pocket expenses:
$0.00

Provide any further details and explain:
Draft practice notes:
1. CgA testing is confounded by proton pump inhibitors and, if testing is necessary, attempts should be made to interrupt therapy where safe prior to requesting CgA testing.
2. CgA levels can vary depending on the assay, and therefore the same assay should be used for the same patient for follow-up tests.

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

Currently, CgA monitoring is funded predominantly on an out-of-pocket basis, with patients typically paying between $45 to $80 per test depending on the provider, with some patients undergoing up to four tests per year as part of disease surveillance. These funding arrangements create inequitable access to testing: uptake is currently contingent on a patient's capacity to pay, and/or their proximity to services willing to absorb costs, which can disproportionately disadvantage people on lower incomes, those in regional and remote areas, and patients requiring more frequent monitoring due to clinical complexity. As a result, access is inconsistent across jurisdictions and providers.

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:

Compared with no biomarker testing, serial CgA monitoring in patients with metastatic NETs who have a trackable (elevated) baseline provides an accessible longitudinal signal of increasing disease activity that can prompt earlier clinical review and confirmatory investigation (CT/MRI and, where appropriate, somatostatin-receptor imaging), thereby supporting timelier reassessment or treatment escalation.

Rising CgA during follow-up is associated with recurrence/progression and can prompt further investigation before new symptoms become apparent (after accounting for confounding factors such as PPI treatment), or the next scheduled scan. In doing so, management changes (e.g. systemic therapy adjustment or locoregional control) may be enacted sooner, potentially improving symptom control, avoiding progression-related complications, and preserving quality of life. This is supported by evidence of the test's performance (pooled sensitivity ~74.6%, specificity ~84.7%). The tests higher specificity but lower sensitivity for RECIST-defined progression supports its utility for triage/trigger rather than a stand-alone rule-out test.

Estimated utilisation

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

Data from the AIHW indicate there were 4,832 new cases of NENs diagnosed in 2021 (18.8 per 100,000, crude rate), and 21,794 prevalent cases of people living with NENs that were diagnosed since 2012. A Victorian audit of NENs from 1982-2019 reported 58% of all NENs were well-differentiated. It is unclear how many of these are likely to have had metastatic disease, as TNM stage was not collected in the NEN dataset for this audit. Applying this percentage to the recent AIHW data yields an estimated 2,802 new cases, and 12,640 prevalence cases in the proposed population, noting that this is likely to be an over-estimate as it does not confirm if these patients had metastatic disease, or if they had a previously resected tumour (and would not be considered in the eligible population).

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

Year 1 estimated uptake (%):
70

Year 2 estimated uptake (%):
80

Year 3 estimated uptake (%):
90

Year 4 estimated uptake (%):
90

Estimate the number of patients who will utilise the proposed technology for the first full year:
10,809

Optionally, provide details:
This estimate is based on the epidemiological estimate for prevalent + incident cases of well-differentiated NENs, multiplied by the expected uptake in year 1 (which often lags behind the availability of a new MBS item). We note, again, that this is likely an overestimate as it does not consider which of these patients had metastatic disease (inclusion criteria), nor if they had radically resected disease (exclusion criteria).

Will the technology be needed more than once per patient?
Yes, multiple times

Over what duration will the health technology or service be provided for a patient? (preferably a number of years):
Lifelong, 1-15+ years based on survival data

Optionally, provide details:
For metastatic NENs, follow-up is generally ongoing/lifelong due to the chronic nature of the condition, and recurrence/progression can occur late in the disease. Of well-differentiated NENs reported in the Victorian audit, the 5-year survival was 86% (95% CI 84-88) and median overall survival was 15.5 years (14.5-NR). It is unclear how generalisable these data are to other States and Territories in the country, particularly those with greater geographical distances that limit access to imaging and other follow-up services compared to Victoria.

What frequency will the health technology or service be required by the patient over the duration? (range, preferably on an annual basis):

1-4 per year

Optionally, provide details:

As noted previously, the COSA guideline recommends 3-monthly CgA testing initially, and then less frequently once stable. Based on available data from labs that currently conduct CgA monitoring in practice, only 7% of patients receive twice-yearly CgA testing, and even fewer patients have more than two CgA tests per year. This may reflect the cost barriers to testing.

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

THE ROYAL COLLEGE OF PATHOLOGISTS OF AUSTRALASIA

PUBLIC PATHOLOGY AUSTRALIA

Entities who request the health technology/service:

MEDICAL ONCOLOGY GROUP OF AUSTRALIA

CLINICAL ONCOLOGY SOCIETY OF AUSTRALIA LIMITED

Private Cancer Physicians of Australia Limited

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

THE ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

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

Cancer Australia

Cancer Council Australia

Consumers Health Forum of Australia Ltd

CANCER VOICES AUSTRALIA

Neuroendocrine Cancer Australia

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

Is the therapeutic good in the process of being considered by the TGA?
No

Please provide details of when you intend to lodge an ARTG inclusion application, or provide a rationale if you do not intend to lodge an ARTG inclusion application:

CgA assays are currently regulated as Class III in-house IVDs, provided by laboratories that are NATA accredited within the scope of this application, for example, PathWest, Sullivan Nicolaides Pathology, SA Pathology, and NSW Health Pathology. These are searchable via the NATA website, and are examples of accredited services, but please note this does not constitute an exhaustive list.