MSAC Application 1767

Immunohistochemistry testing for Claudin 18 expression in patients with gastric or gastro-oesophageal junction cancers, to determine eligibility for PBS subsidised zolbetuximab treatment

Application for MBS eligible service or health technology

MSAC Application Number:
1767

Application title:

Immunohistochemistry testing for Claudin 18 expression in patients with gastric or gastro-oesophageal junction cancers, to determine eligibility for PBS subsidised zolbetuximab treatment.

Submitting organisation:
ASTELLAS PHARMA AUSTRALIA PTY LTD

Submitting organisation ABN:
81147915482

Application description

Succinct description of the medical condition/s:
Gastric or gastroesophageal junction (G/GOJ) cancer (or G/GOJC) comprises cancer that arises from the epithelial lining of the stomach and the gastroesophageal junction (GOJ) (between the stomach and the oesophagus), respectively. Tumours in the GOJ may be classified as either gastroesophageal junction cancer (GOJC) or oesophageal cancer depending on how far from the GOJ they arise. Given the interrelatedness of GC and GOJC, the paucity of data from GOJC as a discrete disease entity, and the fact that patients with GC and GOJC have been the combined target population in clinical trials, data from GC are applied to the G/GOJC population in this dossier when data from GOJC are not available.

The CLDN18.2 protein has been widely studied given its central role in G/GOJC.

Among G/GOJC biomarkers, CLDN18.2 is highly prevalent with quantitative expression studies reporting that approximately 70% of gastric adenocarcinomas express CLDN18.2.

Succinct description of the service or health technology:
The Ventana® CLDN18 (43-14A) RxDx Assay is diagnostic that will be used to assess CLDN18.2 status of gastric cancer patients (HER2 negative with unresectable locally advanced or metastatic G/GOJC) to help determine eligibility for treatment with PBS listed zolbetuximab.

The proposed health technology, Ventana® CLDN18 (43-14A) RxDx Assay, will be used once per patient, per lifetime. It is proposed that one CLDN18.2 test be performed once for each patient as part of the diagnostic biopsy, which is already part of standard management.

There is no known role for CLDN18.2 testing in monitoring a patient's response to zolbetuximab treatment.

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?
Yes

Which list/schedule will the other health technologies be listed on?
Pharmaceutical Benefits Scheme

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.
73342 Prerequisite item

What is the type of service or health technology?
Investigative

Please select the type of investigative health technology:
Histopathology and cytology

PICO Set

Immunohistochemistry testing for Claudin 18 expression in patients with gastric or gastroesophageal junction cancers

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:

Zolbetuximab, a monoclonal antibody targeting claudin-18 isoform 2 (CLDN18.2), is proposed to be funded in combination with fluoropyrimidine- and platinum-containing chemotherapy for the first-line treatment of patients with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastric or gastroesophageal junction adenocarcinoma (G/GOJC) whose tumours are CLDN18.2 positive.

G/GOJ cancer comprises cancer that arises from the epithelial lining of the stomach and the gastroesophageal junction (GOJ) (between the stomach and the oesophagus), respectively. Tumours in the GOJ may be classified as either gastroesophageal junction cancer (GOJC) or oesophageal cancer depending on how far from the GOJ they arise. Given the interrelatedness of GC and GOJC, the paucity of data from GOJC as a discrete disease entity, and the fact that patients with GC and GOJC have been the combined target population in clinical trials, data from GC are applied to the G/GOJC population in this dossier when data from GOJC are not available.

G/GOJC is an important cancer globally, responsible for over one million new cases in 2020 and an estimated 769,000 deaths (equating to one in every 13 deaths globally), ranking 5th for incidence and 4th for mortality. G/GOJC rates are 2-fold higher in men than in women and it is the most commonly diagnosed cancer and the leading cause of cancer death in several South-Central Asian countries. Highest incidence rates are found in Japan and Mongolia, and Eastern Europe, especially compared with North America, Northern Europe, and Africa where rates are relatively low. Early stage G/GOJC is often asymptomatic, and common symptoms in later stage disease are often non-specific; these may include dysphagia, asthenia, indigestion, vomiting, stomach pain, bloating, weight loss, early satiety and/or iron deficiency anaemia.10 The lack of specific or pathognomonic symptoms prevents early diagnosis in the absence of screening programs and it is estimated that 80%–90% of patients in Western countries will present with locally advanced or metastatic tumours that are minimally resectable.

The prognosis for patients with G/GOJC remains poor despite some improvement in survival between 1980 and 2010 following the introduction of a multidisciplinary management approach and the use of palliative chemotherapy . Gastric cancers (including GOJC) have a disproportionate impact on Australians with lower socioeconomic backgrounds, who were 1.4 and 1.5 times more likely to die from GC and OAC respectively in 2012-2016 than the highest socioeconomic group, with even lower survival for Indigenous Australians (AIHW, 2018).

An Australian study by Kumarasinghe et al., 2017 estimated the proportion of G/GOJC patients who are HER2 negative as 86.1%. The proportion of patients ≥ 75% CLDN18.2 expression is estimated 38% from SPOTLIGHT and GLOW.

The PBAC has noted that the clinical need for effective treatments in this therapeutic area is high (Nivolumab PSD Nov 2021, para 7.1, given the poor prognosis for patients and the poor efficacy and high toxicity of current treatments.

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

Name of the proposed health technology:
Ventana® CLDN18 (43-14A) RxDx Assay

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:
Test Comparator: "No testing", as testing for CLDN18.2 is not currently funded, nor available or part of treatment algorithm.

Treatment Comparator: Nivolumab in combination with chemotherapy, for example, FOLFOX (oxaliplatin + folinic acid + fluorouracil) or FOLFIRI (folinic acid, fluorouracil and irinotecan). There is no recommendation for one specific chemotherapy. The choice of regimen depends on patient characteristics, previous treatment and clinician choice.

Outcomes

Outcome description – please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:
The proposed medical service (CLDN18.2 testing) facilitates eligibility to treatment with zolbetuximab and is expected to treat all HER-2 negative, locally advanced or metastatic G/GOJC patients with CLDN18.2 expression greater than or equal to 75%. HER-2 negative, locally-advanced or metastatic G/GOJC patients with CLDN18.2 expression less than or equal to 75% will continue receive nivolumab in combination chemotherapy.

Test-related: Efficacy and safety outcomes of zolbetuximab with and without prior CLDN18.2 testing; Re-biopsy rates.

Test outcomes: Trial based (evidentiary standard) CLDN18.2 IHC assay analytical performance; Comparative performance of CLDN18.2 testing methods; Clinical utility (test plus drug combination).

Healthcare resources: Cost of testing per case; re-biopsy rates; test turn-around time; estimated number of patients being tested.

Proposed MBS items

Proposed Item AAAAA

Proposed category:
PATHOLOGY SERVICES

Proposed group:
P5 - Tissue Pathology

Proposed item descriptor:
Immunohistochemical examination of tumour tissue from a patient diagnosed with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 negative gastric or gastroesophageal junction adenocarcinoma to determine the requirements relating to CLDN18.2 expression (tumour cells ≥75%) for access to zolbetuximab under the Pharmaceutical Benefits Scheme (PBS) are fulfilled.

Proposed MBS fee:
$550.00

Indicate the overall cost per patient of providing the proposed health technology:
$467.50

Please specify any anticipated out of pocket costs:
$82.50

Provide details and explain:
The exact MBS Item fee is to be determined

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

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:
The clinical claim of active (test: Ventana® CLDN18 (43-14A) RxDx Assay plus treatment: VYLOY (zolbetuximab) is that it is non-inferior to comparator of test: no testing of CLDN18.2 plus nivolumab.

Estimated utilisation

Estimate the prevalence and/or incidence of the proposed population:
Number of patients with gastric /GOJ adenocarcinomas who are non-HER2 positive in 2025 is estimated to be 1,325 [redacted]

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

Year 1 estimated uptake (%):
[redacted]

Year 2 estimated uptake (%):
[redacted]

Year 3 estimated uptake (%):
[redacted]

Year 3 estimated uptake (%):
[redacted]

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

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:

- RCPA Quality Assurance Programs Pty Limited

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

- Clinical Oncology Society of Australia Limited
- Gastroenterological Society of Australia
- Medical Oncology Group of Australia
- Private Cancer Physicians of Australia Limited

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

- Australasian Gastro-Intestinal Trials Group
- Clinical Oncology Society of Australia Limited
- Gastroenterological Society of Australia
- Medical Oncology Group of Australia
- Private Cancer Physicians of Australia Limited

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

- Australasian Gastro-Intestinal Trials Group
- GI Cancer Institute

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

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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

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

Codependent details

Will a submission be made to the Pharmaceutical Benefits Advisory Committee (PBAC)?

Yes

Please provide a rationale for the codependency and indicate how the proposed PBS restriction would reference the intervention(s) proposed for MSAC consideration:

It is proposed that all treatment naïve patients diagnosed with HER2-negative locally advanced or metastatic gastric or gastroesophageal junction (G/GOJ) adenocarcinoma will be eligible to undergo testing for CLDN18.2 expression.

Patients who test positive to an CLDN18.2 expression ≥75%, would then be eligible for access to PBS zolbetuximab.

The diagnostic test is proposed to occur at diagnosis of (G/GOJ) adenocarcinoma (rather than following progression) to avoid delays in receiving treatment with zolbetuximab.

The Ventana® CLDN18 (43-14A) RxDx Assay is diagnostic that will be used to assess CLDN18.2 status of HER2 negative with unresectable locally advanced gastric or gastroesophageal junction (G/GOJ) adenocarcinoma) to help determine eligibility for treatment with PBS listed zolbetuximab.

The PBS Restriction for Zolbetuximab would reference the status of CLDN18.2 expression in order to qualify for treatment.

Proposed Elements of the PBS Restriction include:

Clinical criteria:

The condition must be a gastro-oesophageal cancer type as specified in the drug's 'Indications' section of the approved Australian Product Information

AND

The treatment must be prescribed in accordance with the drug's 'Indications' section of the approved Australian Production Information with respect to each of: (i) concomitant drugs/therapies, (ii) line of therapy (i.e. prior treatments, if any),

AND

The condition must have evidence of CLDN18.2 ≥ 75% as demonstrated by immunohistochemistry in tumour material– retain this evidence on the patient's medical records; do not submit a copy of this evidence in this authority application

AND

The condition must have evidence of human epidermal growth factor receptor 2 (HER2) negativity as demonstrated by immunohistochemistry in tumour material– retain this evidence on the patient's medical records; do not submit a copy of this evidence in this authority application