MSAC Application 1782

Genetic testing to detect estrogen receptor 1 (ESR1) mutations in patients with estrogen receptor (ER)-positive, HER2-negative, locally advanced or metastatic breast cancer, to determine eligibility for treatment with PBS subsidised elacestrant

Application for MBS eligible service or health technology

ID:
HPP200167

Application title:
Genetic testing to detect estrogen receptor 1 (ESR1) mutations in patients with estrogen receptor (ER)-positive, HER2-negative, locally advanced or metastatic breast cancer, to determine PBS eligibility for elacestrant (Orserdu®) treatment

Submitting organisation:
A.MENARINI AUSTRALIA PTY LIMITED

Submitting organisation ABN:
62116935758

Application description

Succinct description of the medical condition/s:
Locally advanced or metastatic breast cancer which is estrogen receptor (ER) positive and human epidermal growth factor receptor 2 (HER2)-negative with an activating ESR1 mutation which has progressed following at least one line of hormonal therapy

Succinct description of the service or health technology:
Test to identify estrogen receptor 1 gene (ESR1) activating mutations in patients with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer (a/mBC), who have disease progression following at least one line of endocrine therapy (ET), including a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i), to determine Pharmaceutical Benefits Scheme (PBS) eligibility for elacestrant (Orserdu®),

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.

MBS item number	Selected reason type

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:
Other genetic test

PICO Sets

Application PICO sets

PICO set number	PICO set name
1	Genetic testing to detect estrogen receptor 1 (ESR1) mutations in patients with estrogen receptor (ER)-positive, HER2-negative, locally advanced or metastatic breast cancer, to determine PBS eligibility for elacestrant (Orserdu®) treatment

Genetic testing to detect estrogen receptor 1 (ESR1) mutations in patients with estrogen receptor (ER)-positive, HER2-negative, locally advanced or metastatic breast cancer, to determine PBS eligibility for elacestrant (Orserdu®) treatment

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

Purpose category:
Predictive

Purpose description:
To provide predictive information to support selection of a specific therapy or intervention

Population

Describe the population in which the proposed health technology is intended to be used:
Estrogen receptor 1 gene (ESR1) activating mutations in patients with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer (a/mBC), who have disease progression following at least one line of endocrine therapy (ET), including a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i), to determine Pharmaceutical Benefits Scheme (PBS) eligibility for elacestrant (Orserdu®)

Search and select the most applicable Medical condition terminology (SNOMED CT):
Locally advanced breast cancer

Intervention

Name of the proposed health technology:
Test: Testing for ESR1 mutations in ctDNA extracted from blood (liquid biopsy) to determine eligibility for treatment with elacestrant, a selective estrogen receptor degrader (SERD) to inhibit ER signalling.

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: The nominated comparator is no test

Testing for ESR1 mutation is not currently funded for BC patients, therefore the comparator is no test.

Outcomes

Outcome description – please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:
The EMERALD trial was a multinational, open-label, randomised study comparing the efficacy and safety of elacestrant with SOC ET (fulvestrant or AI) in patients with ER+/HER2- a/mBC previously treated with one or two lines of ET, including a CDK4/6i (Bidard, et al., 2022). In the EMERALD trial, elacestrant demonstrated a statistically significant and clinically meaningful 45% reduction in the risk of progression or death vs. SOC endocrine monotherapy (HR: 0.55; 95% CI: 0.39, 0.77, p=0.0005; median PFS: 3.8 months vs. 1.9 months) in patients with ESR1-mutated tumours (Bidard, et al., 2022). Elacestrant demonstrated long and sustained patient benefit, with 26.8% patients free of progression at 12 months vs. 8.2% in the SOC arm, a 3-fold increment in the rates of patients alive

or free of progression at one year for elacestrant-treated patients vs patients treated with SOC. An absolute increase of 6.7 months in median PFS vs SOC (8.6 months vs.1.9 months) in endocrine sensitive patients with prior CDK4/6i exposure of at least 12 months (71.6% of patients harbouring ESR1-mut tumours in the EMERALD trial) (Kaklamani, et al., 2023; Bardia, et al., 2022; Varella & Cristofanilli, 2023).

Testing for ESR1 mutations in ctDNA extracted from blood (liquid biopsy) is expected to lead to a change in clinical management as patients with a positive result may be eligible to receive treatment with elacestrant. This change is expected to lead to a significant improvement in clinical outcomes, as demonstrated by the pivotal EMERALD trial.

Test outcomes:
Sensitivity, specificity, positivity predictive value (PPV), negative predictive value (NPV).

Treatment outcomes:
• Progression-free survival (PFS)
• Overall survival (OS)
• Overall response rate (ORR), Complete response (CR), partial response (PR), stable disease (SD)
• Duration of response (DR)
• Safety, tolerability

Health care system:
• Cost effectiveness of testing and treatment, financial implications

Proposed MBS items

Proposed Item AAAAA

MBS item number:

Please search and select the proposed category:
PATHOLOGY SERVICES

Please search and select the proposed group:
GENETICS

Please search and select the proposed item descriptor or draft a proposed item descriptor to define the population and health technology usage characteristics that would define eligibility for funding:
A test of ctDNA extracted from blood plasma for the detection of ESR1 missense mutations in an altered tumour, in a patient with:
• locally advanced or metastatic ER-positive, HER2-negative breast cancer who has disease progression following at least one line of endocrine therapy, including a CDK 4/6 inhibitor.
As requested by a specialist or consultant physician, to determine eligibility for treatment with elacestrant under the Pharmaceutical Benefits Scheme (PBS)

Proposed MBS fee:
$0.00

Indicate the overall cost per patient of providing the proposed health technology:
$0.00

Please specify any anticipated out of pocket costs:
$0.00

Provide details and explain:
A detailed utilisation analysis will be presented in the integrated co-dependent MSAC/PBAC submission.

How is the technology/service funded at present? (For example: research funding; State-based funding; self-funded by patients; no funding or payments):
Currently, any testing for ESR1 mutations in ctDNA extracted from blood is self-funded by patients.

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:
Based on the results of the pivotal trial, EMERALD, testing for ESR1 mutations in ctDNA extracted from blood (liquid biopsy) + elacestrant is superior to no testing + SOC 2L+ treatment, including ET.

Estimated utilisation

Estimate the prevalence and/or incidence of the proposed population:
ESR1 mutations affect up to 40% of ER+ cases previously treated with ET in the metastatic setting

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:
TBC

Optionally, provide details:
A detailed utilisation analysis including prevalence and estimated will be presented in the integrated co-dependent MSAC/PBAC submission.

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):
At each point of disease progression

Optionally, provide details:
ESR1 mutations often emerge at the time of first or subsequent progressions post ET/AI treatment. The frequency of ESR1 mutations changes during the course of the disease and therefore testing for ESR1 mutations is relevant at each progression during the metastatic treatment course

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

Optionally, provide details:
ESR1 mutations often emerge at the time of first or subsequent progressions post ET/AI treatment. The frequency of ESR1 mutations changes during the course of the disease and therefore testing for ESR1 mutations is relevant at each progression during the metastatic treatment course

Consultation

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

Professional body name:
Royal College of Pathologists of Australasia

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

Professional body name:
CLINICAL ONCOLOGY SOCIETY OF AUSTRALIA LIMITED

Professional body name:
Medical Oncology Society of Australia (MOGA)

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

Professional body name:
Cancer Nurses Society of Australia

Professional body name:
COSA Cancer Pharmacists Group

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

Number of organisations listed: 3
Professional body name:
BREAST CANCER NETWORK AUSTRALIA

Number of organisations listed: 3
Professional body name:
National Breast Cancer Foundation (NBCF)

Number of organisations listed: 3
Professional body name:
Rare Cancers Australia Ltd (RCA)

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

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?
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:
The application requests Medicare Benefits Schedule (MBS) funding for testing to identify estrogen receptor 1 gene (ESR1) activating mutations in patients with estrogen receptor (ER)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer (a/mBC), who have disease progression following at least one line of endocrine therapy (ET), including a cyclin-dependent kinase 4/6 inhibitor (CDK4/6i), to determine Pharmaceutical Benefits Scheme (PBS) eligibility for elacestrant (Orserdu®), a new generation, selective estrogen receptor degrader (SERD) to inhibit ER signalling.

The PBS restriction for Orserdu (elacestrant) will specify use in patients who test positive for ESR1 activating mutations