

MSAC Application 1783

Genetic testing to detect PIK3CA mutations in patients with hormone receptor (HR)-positive, HER-2 negative, locally advanced or metastatic breast cancer, to determine eligibility for treatment with PBS subsidised inavolisib

PICO Set Document

Population

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

Adults (≥ 18 years of age) with hormone receptor-positive (HR+), HER2-negative (HER2-) locally advanced or metastatic breast cancer.

Specify any characteristics of patients with, or suspected of having, the medical condition, who are proposed to be eligible for the proposed health technology, describing how a patient would be investigated, managed and referred within the Australian healthcare system in the lead up to being considered eligible for the technology:

Prior to being considered for PIK3CA testing, patients would receive clinical consultations and undergo physical examinations and collection of clinical history. Where breast cancer is suspected the following investigations are anticipated:

- Biopsy of suspected cancerous tissue, followed by pathological review to confirm or exclude a diagnosis of breast cancer
- Diagnostic imaging (computed tomography or magnetic resonance imaging) of the chest and abdomen, and bone scintigraphy to support disease staging
- Pathological assess of therapeutically relevant biomarkers
 - Biomarkers recommended to be assessed in all patients with newly diagnosed or recurrent breast cancer in ESMO Guidelines (Gennari et al. 2021) are: oestrogen receptor (ER), progesterone receptor (PgR) and human epidermal growth factor receptor 2 (HER2).

The diagnostic work up of a patient with suspected breast cancer involves a multidisciplinary team. This would typically involve a general practitioner, medical oncologist, radiologist and pathologist.

Initial consultations and referrals for diagnostic imaging and pathological investigations may be coordinated by a general practitioner. In most cases, or if the general practitioner is not experienced in the management of breast cancer patients, a patient is referred to a specialist medical oncologist to oversee the diagnostic work up and ongoing management may occur.

As per the proposed population, patients would receive investigations required to establish a diagnosis of HR+, HER2- locally advanced or metastatic breast cancer prior to being considered eligible for PIK3CA testing.

Provide a rationale for the specifics of the eligible population:

This application relates to a co-dependent technology where the outcome of PIK3CA testing is used to identify patients eligible for treatment with inavolisib (plus palbociclib and fulvestrant) through the Pharmaceutical Benefits Scheme (PBS).

The efficacy and safety of inavolisib has been assessed in the INAVO120 trial. Key eligibility criteria for enrolment in the INAVO120 trial were:

- Aged ≥ 18 years of age
- Confirmed diagnosis of HR+/HER2- breast cancer
- Metastatic or locally advanced disease not amenable to curative therapy.

The rationale for the specifics of the eligible population is to ensure consistency in the circumstances of use of PIK3CA testing and treatment with inavolisib funded through the Medicare Benefits Schedule (MBS) and PBS respectively with the use of PIK3CA testing and treatment with inavolisib in the INAVO120 trial.

Are there any prerequisite tests?

Yes

Testing to determine hormone receptor and HER2 status would be required prior to patients being eligible for PIK3CA testing in the proposed population.

Are the prerequisite tests MBS funded?

Yes

Hormone receptor (oestrogen and progesterone) and c-erb-B2 (HER2) testing by immunohistochemical examination of biopsy material is funded through MBS items 72848/73061.

Provide details to fund the prerequisite tests:

Provide a response if you answered 'No' to the question above

Intervention

Name of the proposed health technology:

Testing for PIK3CA mutation status using a next generation sequencing (NGS) assay.

Per-protocol the assessment of PIK3CA mutation status in the INAVO120 trial could be performed by testing circulating tumour DNA (ctDNA) derived from a blood sample drawn from the patient or testing of a tumour tissue sample.

Describe the key components and clinical steps involved in delivering the proposed health technology:

There are no material differences in the steps involved in the identification of PIK3CA mutations using a NGS assay compared with the identification of mutations in other genes (e.g. identification of EGFR mutations) using a NGS assay.

The key steps undertaken in the assessment of genetic mutations using a NGS assay are:

- DNA and/or RNA is isolated from a plasma sample (ctDNA analysis) or formalin-fixed, paraffin-embedded tumour sample (tissue analysis)
- Preparation of sequencing libraries
- Enrichment of sequencing libraries for genes of interest (notably PIK3CA)
- Analysis and reporting of test results to referring clinician.

Identify how the proposed technology achieves the intended patient outcomes:

Inavolisib: Inavolisib is a selective inhibitor of the Class I PI3K α isoform and belongs to the PI3K inhibitor class of drugs.

Inavolisib exerts its activity by binding to the adenosine 5'-triphosphate binding site of p110 α . In-vivo studies demonstrated that inavolisib specifically degrades mutant p110 α , inhibits proliferation and induces apoptosis in PIK3CA-mutant breast cancer cell lines, and inhibits with increased potency in tumour cell bearing mutant p110 α over cell bearing wild type p110 α (Hanan et al. 2022).

Based on its mechanism of action (PIK3 inhibitor) and the results of preclinical studies reporting increased potency in tumour cells bearing mutant p110 α , clinical trials have been designed to assess the safety and efficacy of inavolisib only in patients assessed as harbouring PIK3CA mutations.

PIK3CA testing: The identification of PIK3CA mutations through PIK3CA testing is intended to improve patient outcomes by identifying a subgroup of patients (PIK3CA mutated) being considered for treatment for HR+/HER2-locally advanced or metastatic breast cancer that are likely to be sensitive to treatment with the PIK3CA inhibitor inavolisib.

Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components?

Inavolisib: Yes

PIK3CA testing: No

Explain whether it is essential to have this trademark component or whether there would be other components that would be suitable:

Consistent with the PBS listing of medicines, the foreshadowed PBS restriction for inavolisib will be specific to the trademarked component (inavolisib).

The proposed MBS items descriptors do not specify the use of a trademarked assay for the conduct of PIK3CA mutation testing.

Are there any proposed limitations on the provision of the proposed health technology delivered to the patient (For example: accessibility, dosage, quantity, duration or frequency):

Yes

It is proposed that PIK3CA testing funded through the MBS would be applicable only once per lifetime. This limitation is consistent with other biomarker tests performed for the purpose of establishing patient eligibility to access targeted treatment through the PBS.

Provide details and explain:

Provide a response if you answered 'No' to the question above

If applicable, advice which health professionals will be needed to provide the proposed health technology:

The conduct of PIK3CA testing would be performed in a pathology laboratory by a molecular pathologist, or laboratory staff working under the direct supervision of the pathologist.

If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:

Not applicable.

If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:

A general practitioner or medical oncologist would provide the referral for pathological assessments associated with informing decisions on treatment selection in patients with locally advanced or metastatic breast cancer.

When hormone receptor and HER2 testing is performed by an anatomical pathologist, or in a laboratory without the equipment required to perform NGS analysis, a pathologist may refer PIK3CA testing to a specialty molecular pathology laboratory.

Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?

Yes

Provide details and explain:

All personnel performing molecular pathology testing must be suitably qualified and testing laboratories must hold the appropriate accreditations to offer pathology testing in Australia. These training and accreditation requirements apply to all cancer biomarker testing and are not specific to PIK3CA testing.

Several private and public pathology laboratories are already providing PIK3CA testing services in Australia^{1,2}. As such, no additional training or accreditation requirements are associated with this application.

Indicate the proposed setting(s) in which the proposed health technology will be delivered:

- Consulting rooms
- Day surgery centre
- Emergency Department
- Inpatient private hospital
- Inpatient public hospital
- Laboratory
- Outpatient clinic
- Patient's home
- Point of care testing
- Residential aged care facility
- Other (please specify)

¹ <https://www.clinicallabs.com.au/cancer-services/breast-cancer/>

² <https://www.petermac.org/health-professionals/services-for-health-professionals/pathology-health-professionals/molecular-pathology/somatic-testing>

Is the proposed health technology intended to be entirely rendered inside Australia?

Yes

Provide additional details on the proposed health technology to be rendered outside of Australia:

Provide a response if you answered 'No' to the question above

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

Comparators are nominated for the PIK3CA testing and inavolisib components:

- For the PIK3CA testing component, the nominated comparator is no PIK3CA testing
- For the inavolisib component, the nominated comparator is palbociclib plus fulvestrant.

List any existing MBS item numbers that are relevant for the nominated comparators:

There are no existing MBS items numbers relevant for the nominated comparator of no PIK3CA testing.

Palbociclib and fulvestrant are both currently funded through the PBS as treatment for patients with HER+/HER2- locally advanced or metastatic breast cancer (Table 1).

Table 1: PBS codes for palbociclib and fulvestrant (comparator treatment regimen)

Treatment	PBS code(s)
Palbociclib	12822W, 12818P, 12819Q
Fulvestrant	12300J

Provide a rationale for why this is a comparator:

PIK3CA testing: While not reimbursed through the MBS, PIK3CA testing in breast cancer patients is currently being undertaken in several private and public molecular pathology laboratories. As such, it is reasonable to claim that, to some extent, PIK3CA testing represents established practice.

As outlined in the Medical Services Advisory Committee (MSAC) Guidelines “in situations where the health technology proposed for public funding is already established practice (i.e. it has already ‘diffused’), the comparator should be what was used before the introduction of the health technology” (MSAC 2021 p. 36).

The nomination of ‘no PIK3CA testing’ aligns with the approach to comparator selection outlined in the MSAC Guidelines in that it reflects what was used before the introduction of PIK3CA testing.

Inavolisib: In the INAVO120 trial patients were randomised to receive inavolisib in combination with palbociclib plus fulvestrant or placebo in combination with palbociclib plus fulvestrant.

The choice of clinical trial comparator (palbociclib plus fulvestrant) represents a preferred first line treatment regimen for HR+/HER2- metastatic or advanced breast cancer (NCCN 2024). Palbociclib (a CDK 4/6 inhibitor) and fulvestrant are both listed on the PBS and would be required to be used in combination with inavolisib in patients identified with PIK3CA mutations through the foreshadowed PBS restriction for inavolisib presented to the Pharmaceutical Benefits Advisory Committee (PBAC).

Nomination of palbociclib plus fulvestrant as the comparator treatment regimen will allow the PBAC to assess the incremental safety and effectiveness of adding inavolisib to palbociclib plus fulvestrant in patients with HR+/HER2-/PIK3CA mutated locally advanced or metastatic breast cancer.

Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator?

- None (used with the comparator)
- Displaced (comparator will likely be used following the proposed technology in some patients)
- Partial (in some cases, the proposed technology will replace the use of the comparator, but not all)
- Full (subjects who receive the proposed intervention will not receive the comparator)

Outline and explain the extent to which the current comparator is expected to be substituted:

When requested, PIK3CA testing would fully replace the comparator of no PIK3CA testing.

When prescribed, inavolisib would be used with comparator of palbociclib plus fulvestrant.

Outcomes

List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator):

- Health benefits

Major outcome: Progression free survival

Major outcome: Overall survival

Minor outcome: Objective response rate

Minor outcome: Best overall response

Minor outcome: Duration of response

Minor outcome: Clinical benefit rate

Minor outcome: Health-related quality of life

- Health harms

Major outcome: Rate and nature of adverse events reported in patients treated with inavolisib in combination with palbociclib plus fulvestrant vs placebo in combination with palbociclib plus fulvestrant.

- Resources
- Value of knowing

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

A change in management is expected as a result of the test information. Patients identified as harbouring a PIK3CA mutation would be eligible for treatment with inavolisib (used in combination with palbociclib plus fulvestrant). Patients with no PIK3CA mutations identified would not be eligible for inavolisib and, subsequently, managed with palbociclib plus fulvestrant or other CDK 4/6 inhibitor plus fulvestrant or aromatase inhibitor based on individual patient circumstances.

Proposed MBS items

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

PIK3CA testing in breast cancer patients is currently being undertaken in several private and public molecular pathology laboratories. Under these arrangements, testing would either be self-funded by patients or funded through State-based programs.

For patients being managed in clinics registered as investigational sites for breast cancer clinical trials, PIK3CA testing may be performed through research funding or supported by the sponsor of the clinical trial.

Provide at least one proposed item with their descriptor and associated costs, for each Population/Intervention:

Alternate listing scenarios supporting the conduct of PIK3CA testing through the MBS are presented for consideration by the Department of Health and Aged Care.

The applicant will present an MBS item descriptor in any forthcoming reimbursement submission based on advice from the Department of Health and Aged Care on its preferred approach to funding PIK3CA testing.

Scenario 1: Amend the MBS item descriptor presented in MSAC Application 1766

The applicant notes that MSAC Application 1766 is requesting funding for detection of AKT-pathway altered tumour to determine eligibility for treatment with an AKT serine/threonine kinase inhibitor (capivasertib) under the PBS (MSAC Application 1766 (2024)).

Minor amendment (bold text in table below) to the MBS item descriptor set out in the PICO Set Document for MSAC Application 1766 would facilitate patient access to PIK3CA testing as performed in the INAVO120 trial.

MBS item number (where used as a template for the proposed item)	Table 1 (p. 8) of PICO Set Document for MSAC Application 1766
Category number	Category 6 – Pathology Services
Category description	Group P7 - Genetics
Proposed item descriptor	<p>A test of tumour tissue or circulating tumour DNA (ctDNA) for the detection of an AKT-pathway altered (PIK3CA, AKT1 or PTEN) tumour, in a patient with:</p> <ul style="list-style-type: none"> locally advanced (inoperable) or metastatic hormone receptor positive, HER2-negative breast cancer <p>As requested by a specialist or consultant physician, to determine eligibility for treatment with an AKT serine/threonine kinase inhibitor or PIK3CA inhibitor under the Pharmaceutical Benefits Scheme (PBS)</p>
Proposed MBS fee	No MBS fee proposed in MSAC Application 1766
Indicate the overall cost per patient of providing the proposed health technology	MSAC Application 1766 states that “a detailed utilisation analysis will be presented in the integrated co-dependent MSAC/PBAC submission”
Please specify any anticipated out of pocket expenses	MSAC Application 1766 states that “a detailed utilisation analysis will be presented in the integrated co-dependent MSAC/PBAC submission”
Provide any further details and explain	MSAC Application 1766 states that “a detailed utilisation analysis will be presented in the integrated co-dependent MSAC/PBAC submission”

Scenario 2: Create an MBS item descriptor specific to PIK3CA testing and PIK3CA inhibitor (inavolisib) access

MBS item number (where used as a template for the proposed item)	MBS item 73433 was used as a high-level template for the proposed item
Category number	Category 6 – Pathology Services
Category description	Group P7 - Genetics
Proposed item descriptor	<p>Next generation sequencing (NGS) test for phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform (PIK3CA) mutations performed on tumour tissue or circulating tumour DNA (ctDNA) from a patient with locally advanced (inoperable) or metastatic breast cancer, if:</p> <ul style="list-style-type: none"> (a) The breast cancer is documented as hormone receptor-positive; and (b) The breast cancer is documented as HER2-negative; and (c) The test is requested by a specialist or consultant physician to determine if requirements relating to PIK3CA mutation status for access to a PIK3CA inhibitor under the Pharmaceutical Benefits Scheme are fulfilled <p>Applicable only once per lifetime</p>
Proposed MBS fee	<p>The applicant is currently engaging with molecular pathology laboratories to understand the costs associated with PIK3CA testing.</p> <p>It is foreshadowed that an MBS fee of \$350 - \$400 will be proposed. However, the proposed MBS fee will be determined by the costing information gathered during the preparation of any forthcoming reimbursement submission.</p>
Indicate the overall cost per patient of providing the proposed health technology	\$350 - \$400 (indicative cost only)
Please specify any anticipated out of pocket expenses	<p>\$0</p> <p>PIK3CA testing is currently being offered by several private and public molecular pathology laboratories at a fee of \$350 - \$400. A MBS funded item in the same price range will minimise the potential for out of pocket expenses.</p>

Algorithms

PREPARATION FOR USING THE HEALTH TECHNOLOGY

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:

As outlined previously, patients would undergo consultations and investigations (pathological assessment of tumour tissue and diagnostic imaging) required to establish a diagnosis of HR+/HER2- locally advanced or metastatic breast cancer.

Is there any expectation that the clinical management algorithm before the health technology is used will change due to the introduction of the proposed health technology?

No

Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:

Please provide a response if you answered 'Yes' to the question above

USE OF THE HEALTH TECHNOLOGY

Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:

The collection of a biopsy sample for the purpose of undertaking pathologic assessment of tumour tissue is routine clinical practice. For a small number of patients whose original biopsy sample may have been of insufficient quality, or was exhausted through performing prior pathological assessment, a re-biopsy may be required to obtain adequate tumour tissue to perform PIK3CA testing.

For patients having PIK3CA testing performed on ctDNA, collection of a plasma sample for processing and testing is required. This could be performed during a consultation with the clinician requesting PIK3CA testing or at a pathology collection centre, with the sample subsequently transported to the pathology laboratory for processing and testing.

Explain what other healthcare resources are used in conjunction with the comparator health technology:

Fulvestrant is administered by intramuscular injection, with the recommended dose (500 mg) to be administered as 2 x 5 mL injections, one in each buttock, over a 1 – 2 minutes/injection. Healthcare resources associated with an intramuscular injection of fulvestrant by a clinician or nurse would be used with the comparator health technology of palbociclib and fulvestrant

Inavolisib is taken orally and is intended to be used in combination with palbociclib (also taken orally) and fulvestrant. Therefore, no incremental difference in healthcare resources associated with treatment administration are anticipated.

Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:

Healthcare resource	Testing component		Treatment component	
	PIK3CA testing (Proposed)	No PIK3CA testing (Comparator)	Inavolisib in combination with palbociclib and fulvestrant (Proposed)	Palbociclib and fulvestrant (Comparator)
PIK3CA testing	✓	✗	NA	NA
Re-biopsy to collect fresh tissue for testing	✓ (only in patients with inadequate tissue from original biopsy)	✗	NA	NA
Collection of plasma sample for testing	✓ (only in patients requested for ctDNA testing)	✗	NA	NA
Clinical or nurse consultation for treatment administration	NA	NA	✓	✓

CLINICAL MANAGEMENT AFTER THE USE OF HEALTH TECHNOLOGY

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, *after* the use of the proposed health technology:

Inavolisib would be used in addition to palbociclib and fulvestrant in patients assessed as harbouring PIK3CA mutations.

Patients whose tumour is assessed as not harbouring PIK3CA mutations would not be eligible for treatment with inavolisib through the PBS.

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, *after* the use of the comparator health technology:

Patients who do not undergo PIK3CA will have an unknown PIK3CA mutation status and would not be indicated for treatment with inavolisib. Treatment with palbociclib plus fulvestrant or other CDK 4/6 inhibitor plus fulvestrant or aromatase inhibitor regimen is indicated.

Describe and explain any differences in the healthcare resources used after the proposed health technology vs. the comparator health technology:

Healthcare resource	Testing component		Treatment component	
	PIK3CA testing (Proposed)	No PIK3CA testing (Comparator)	Inavolisib in combination with palbociclib and fulvestrant (Proposed)	Palbociclib and fulvestrant (Comparator)
Inavolisib	✓ (only in patients harbouring a PIK3CA mutation)	✗	✓	✗

Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:

Figure 1: Clinical management algorithm without PIK3CA testing and inavolisib

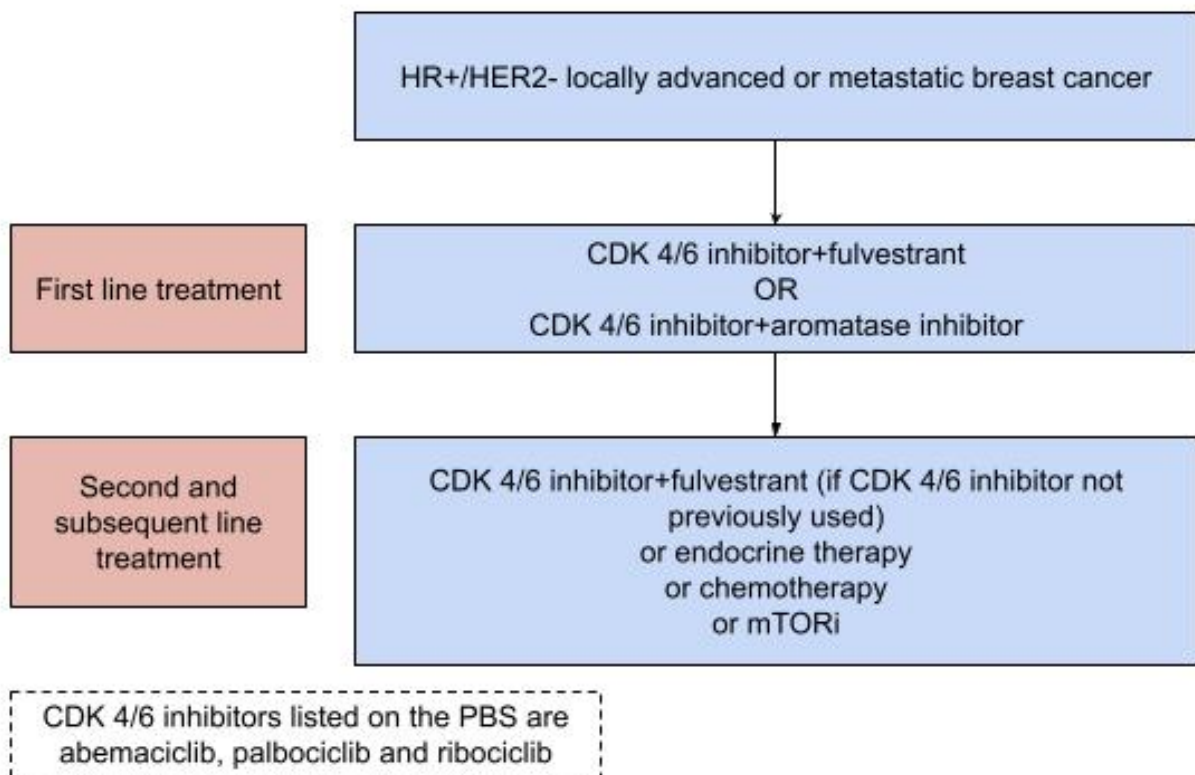
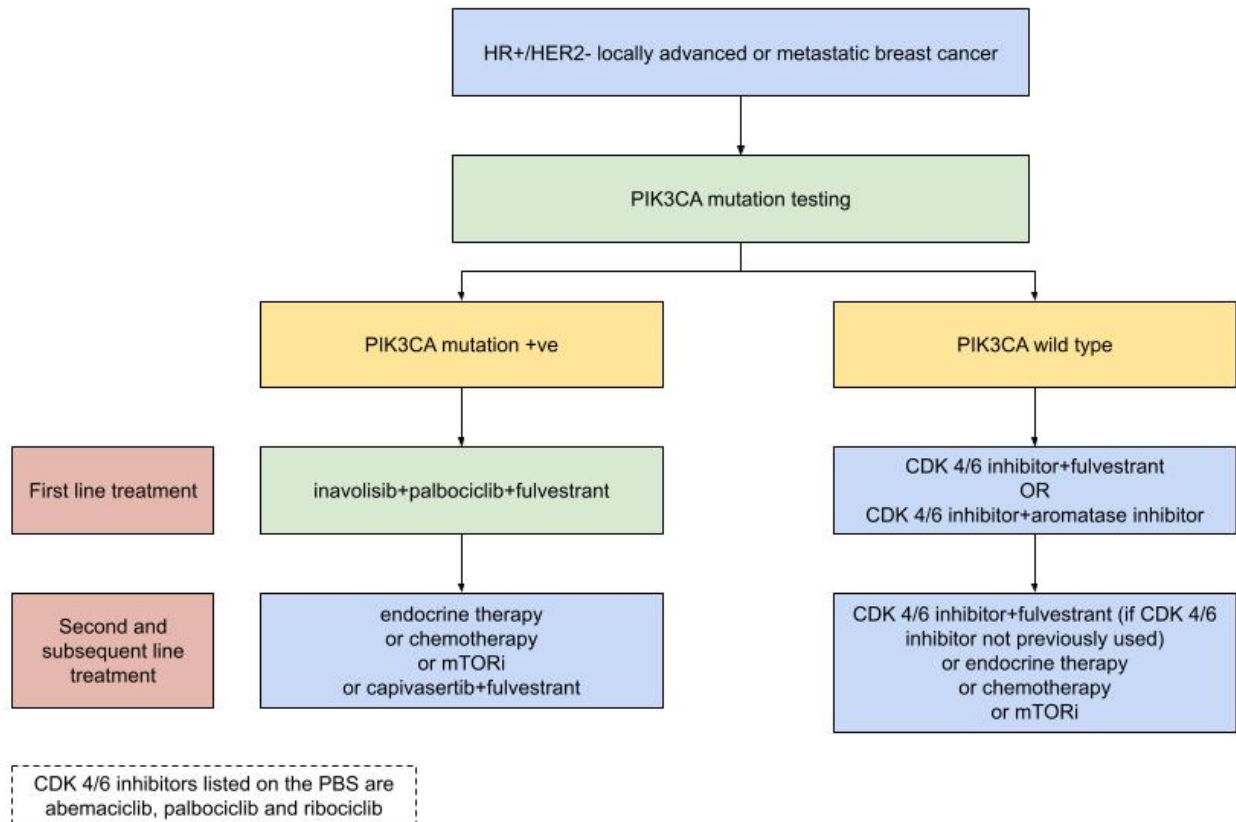


Figure 2: Clinical management algorithm with PIK3CA testing and inavolisib



Notes: Green shaded boxes highlight proposed changes to current pathway. The outcome of PIK3CA mutation testing is highlighted in yellow.

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
 Non-inferior
 Inferior

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

The overall claim is that PIK3CA testing followed by inavolisib in combination with palbociclib and fulvestrant in patients with PIK3CA mutations is superior to no PIK3CA testing and treatment with palbociclib plus fulvestrant.

The clinical claim is supported by the results of the INAVO120 trial where improvements in progression free survival and overall survival were reported for patients treated with inavolisib (Table 2). All patients enrolled in the INAVO120 trial were assessed as having PIK3CA mutations by testing of tumour tissue or ctDNA.

Table 2: Progression free survival and overall survival reported at primary analysis of INAVO12 trial

Outcome	Inavolisib in combination with palbociclib and fulvestrant (N= 161)	Palbociclib and fulvestrant (N= 164)
Progression free survival		
Months, Median (95% CI)	15.0 (11.3, 20.5)	7.3 (5.6, 9.3)
Hazard ratio (95% CI)	0.43 (0.32, 0.59), p<0.0001	
Overall survival		
Months, Median (95% CI)	NE (27.3, NE)	31.1 (22.3, NE)
Hazard ratio (95% CI)	0.64 (0.43, 0.97), p=0.0338	

Abbreviations: CI=confidence interval; NE=not estimable

Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?

Per the results of the INAVO120 trial, patients with PIK3CA mutations treated with inavolisib had improved progression survival and overall survival compared with palbociclib plus fulvestrant alone.

It is foreshadowed that the PBS restriction for inavolisib will include a criterion that a patient must be assessed as harbouring a PIK3CA mutation to be eligible for treatment with inavolisib. As such, requestors would seek to use PIK3CA testing for the purpose of assessing patient eligibility to access inavolisib through the PBS.

Identify how the proposed technology achieves the intended patient outcomes:

Please refer to the response to the same question that was provided in the Intervention section.

For some people, compared with the comparator(s), does the test information result in:

A change in clinical management? Yes

A change in health outcome? Yes

Other benefits? No

Please provide a rationale, and information on other benefits if relevant:

Provide your response here

In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator?

- More costly
- Same cost
- Less costly

Provide a brief rationale for the claim:

Additional costs are incurred through the conduct of PIK3CA testing and the addition of inavolisib to palbociclib plus fulvestrant in patients assessed as harbouring a PIK3CA mutation.

Summary of Evidence

Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology. At 'Application Form lodgement'

	Type of study design	Title of journal article or research project	Short description of research**	Website link to journal article or research	Date of publication
1.	Phase 3 trial	Inavolisib or placebo in combination with palbociclib and fulvestrant in patients with PIK3CA-mutated, HR+, HER2-locally advanced or metastatic breast cancer: Phase III INAVO120 primary analysis NCT04191499	Primary analysis of the trial reported a statistically significant and clinically improvement in PFS in patients with a PIK3CA mutation treated with inavolisib: HR 0.43 (95% CI 0.32, 0.59), P<0.001 Per-protocol PIK3CA testing was performed on ctDNA or tumour tissue during the screening phase	https://medically.roche.com/content/dam/pdmahub/restricted/oncology/sabcs-2023/SABCS-2023-presentation-jhaveri-inavolisib-or-placebo-in-combination-with-palbociclib.pdf	2023

	Type of study design	Title of journal article or research project	Short description of research**	Website link to journal article or research	Date of publication
2.	Meta-analysis	Prognostic effects of PIK3CA mutation status on progression and survival	<p>Outcomes from 11 trials with a total of 3,219 patients were pooled (PIK3CA mutated=1,386; PIK3CA wild type=1,883).</p> <p>In patients with HR+/HER2-breast cancer, PIK3CA mutation was associated with shorter PFS (-1.8 months) and shorter OS (-8.4 months). This meta-analysis is suggestive of PIK3CA mutations having a negative prognostic value</p>	https://pubmed.ncbi.nlm.nih.gov/36131248/	2022
3.	NGS assay clinical development and validation study	Clinical and analytical validation of FoundationOne Liquid CDx, a novel 324-Gene ctDNA-based comprehensive genomic profiling assay for cancers of solid tumour origin	<p>Describes the development and valuation of the FoundationOne Liquid CDx assay. This assay was used to perform ctDNA testing in the INAVO120 trial.</p> <p>A clinical bridging study of PIK3CA testing using FoundationOne CDx and the tumour tissue PCR assay used in the SOLAR-1 trial (alpelisib). Across 375 samples analysed a PPA of 72% and NPA of 100% for the detection of PIK3CA mutations was reported</p>	https://pubmed.ncbi.nlm.nih.gov/32976510/	

	Type of study design	Title of journal article or research project	Short description of research**	Website link to journal article or research	Date of publication
4.	Review	A systematic review of the prevalence and diagnostic work up of PIK3CA mutations in HR+/HER2- metastatic breast cancer	Evidence from 39 studies was synthesised to estimate the prevalence of PIK3CA mutations (median 36%; IQR 31%, 46%). Concordance of PIK3CA testing between ctDNA and tumour tissue was reported in 6 studies. Concordance ranged from 70% to 94%	https://pubmed.ncbi.nlm.nih.gov/32637176/	2020

Abbreviations: HR+=hormone receptor positive; HER2-= human epidermal growth factor receptor 2 negative; ctDNA=circulating tumour DNA; PFS=progression free survival; OS=overall survival; PPA=positive percent agreement; NPA=negative percent agreement; IQR=interquartile range