Australian Government

Department of Health

Application Form

(New and Amended Requests for Public Funding)

(Version 2.5)

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires in order to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Guidelines to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted.

The application form will be disseminated to professional bodies / organisations and consumer organisations that have will be identified in Part 5, and any additional groups that the Department deem should be consulted with. The application form, with relevant material can be redacted if requested by the Applicant.

Should you require any further assistance, departmental staff are available through the contact numbers and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

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Fax: +61 2 6289 5540
Email: hta@health.gov.au
Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant): N/A
Corporation name: **Redacted**
ABN: **Redacted**
Business trading name: **Redacted**

Primary contact name: Natalie Betts, Senior Health Economist

Primary contact numbers
Business: **Redacted**
Mobile: **Redacted**
Email: **Redacted**

Alternative contact name: Rachael Anderson, Health Economics & Pricing Manager

Alternative contact numbers
Business: **Redacted**
Mobile: **Redacted**
Email: **Redacted**

2. (a) Are you a consultant acting on behalf of an Applicant?

☐ Yes
☒ No

(b) If yes, what is the Applicant(s) name that you are acting on behalf of?

Insert relevant Applicant(s) name here.

3. (a) Are you a lobbyist acting on behalf of an Applicant?

☐ Yes
☒ No

(b) If yes, are you listed on the Register of Lobbyists?

☐ Yes
☐ No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

4. Application title

Testing for epidermal growth factor receptor (EGFR) status in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) to determine eligibility for osimertinib.

5. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Lung cancer is the second-leading cause of premature death for all Australians. It is the fifth most commonly diagnosed cancer in Australia and one of the most lethal cancer types, with a five-year survival rate of only 16%.[1] Non-small cell lung cancer accounts for over 80% of all lung cancer cases, and is usually diagnosed at an advanced stage when it is no longer amenable to surgical resection.[2] In approximately 15% of NSCLC patients, the tumour harbours a mutation in the EGFR gene, which confers sensitivity to EGFR tyrosine kinase inhibitors (EGFR TKIs).[3] First and second-generation EGFR TKIs such as gefitinib and erlotinib are PBS-listed for this indication with a corresponding MBS item to determine eligibility (Item 73337). However, more than 50% of patients on these therapies develop acquired resistance to treatment with progression of disease after approximately 9 to 13 months.[4-6] There is an unmet need for a therapy that can prolong the time to development of resistance, improving survival and quality of life.

6. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

In patients with NSCLC, EGFR mutation testing is well established as part of the diagnosis and classification pathway since the test (MBS Item 73337) and EGFR TKI therapies (gefitinib and erlotinib) have been publicly funded. Testing for EGFR gene mutation in patients with locally advanced or metastatic NSCLC involves: (i) collection of an appropriate sample of lung cancer tissue for testing; (ii) preparation of the tissue sample; and (iii) testing the prepared sample for an activating mutation of the EGFR gene. This application does not nominate a specific methodology for EGFR mutation testing, rather requests a minor amendment to the existing MBS item for EGFR mutation testing (Item 73337) to include osimertinib. There will be no increase in the number of tests or cost to the MBS as a result of the amended listing.

A previous application was submitted for an additional EGFR mutation test (EGFR T790M mutation) to determine subsidised access to osimertinib in the second-line setting (following disease progression after first-line EGFR TKI; Application 1407). This application requests EGFR mutation testing to determine subsidised access to osimertinib in the first-line setting. A T790M mutation test is not required in the first-line setting.

7. (a) Is this a request for MBS funding?

☒ Yes
☐ No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

☒ Amendment to existing MBS item(s)
☐ New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service:

MBS Item 73337

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

i. ☐ An amendment to the way the service is clinically delivered under the existing item(s)
ii. ☐ An amendment to the patient population under the existing item(s)
iii. ☐ An amendment to the schedule fee of the existing item(s)

iv. ☐ An amendment to the time and complexity of an existing item(s)
v. ☐ Access to an existing item(s) by a different health practitioner group
vi. ☒ Minor amendments to the item descriptor that does not affect how the service is delivered
vii. ☐ An amendment to an existing specific single consultation item
viii. ☐ An amendment to an existing global consultation item(s)
ix. ☐ Other (please describe below):

Insert description of 'other' amendment here

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i. ☐ A new item which also seeks to allow access to the MBS for a specific health practitioner group
ii. ☐ A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
iii. ☐ A new item for a specific single consultation item
iv. ☐ A new item for a global consultation item(s)

(f) Is the proposed service seeking public funding other than the MBS?

☐ Yes
☒ No

No other source of public funding for EGFR testing other that the MBS will be sought. However, this application will be part of a co-dependent submission where public funding on the PBS for osimertinib will be sought for eligible patients.

(g) If yes, please advise:

N/A

8. What is the type of service:

☐ Therapeutic medical service
☐ Investigative medical service
☐ Single consultation medical service
☐ Global consultation medical service
☐ Allied health service
☒ Co-dependent technology
☐ Hybrid health technology

9. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

i. ☐ To be used as a screening tool in asymptomatic populations
ii. ☐ Assists in establishing a diagnosis in symptomatic patients
iii. ☐ Provides information about prognosis
iv. ☒ Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
v. ☐ Monitors a patient over time to assess treatment response and guide subsequent treatment decisions
vi. ☐ Is for genetic testing for heritable mutations in clinically affected individuals and, when also appropriate, in family members of those individuals who test positive for one or more relevant mutations (and thus for which the Clinical Utility Card proforma might apply)

10. Does your service rely on another medical product to achieve or to enhance its intended effect?

☒ Pharmaceutical / Biological
☐ Prosthesis or device
☐ No

11. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

☐ Yes
☒ No

(b) If yes, please list the relevant PBS item code(s):

Insert PBS item code(s) here

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

☒ Yes (please provide PBAC submission item number below)
☐ No

PBAC submission will be submitted as part of a co-dependent application.

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Trade name: TAGRISSO®
Generic name: osimertinib

12. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List? N/A

☐ Yes
☐ No

(b) If yes, please provide the following information (where relevant):

Billing code(s): Insert billing code(s) here
Trade name of prostheses: Insert trade name here
Clinical name of prostheses: Insert clinical name here
Other device components delivered as part of the service: Insert description of device components here

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

☐ Yes
☐ No

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

☐ Yes
☐ No

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

Insert sponsor and/or manufacturer name(s) here

13. Please identify any single and / or multi-use consumables delivered as part of the service?

Australian molecular pathology service providers currently use a number of different commercial test kits and locally developed methods for EGFR mutation testing with the majority based on established reverse transcription polymerase chain reaction (RT-PCR) or next generation sequencing (NGS) methods. The consumables delivered as part of the service include the following.

- Sanger Sequencing requires simple reagents
- Companion Diagnostics (RT-PCR systems) require Extraction Kit; Quantification Kit; and EGFR Kit for each specific platform (Roche for cobas & Qiagen for Pyrosequencing)
- NGS - Extraction Kit; Quantification Kit and Panel specific to each NGS (Ion Torrent & Illumina). These panels often cover 26+ genes and can cover EGFR, KRAS, BRAF concurrently. (Most labs use Qiagen kits for extraction and Quantification)

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

14. (a) If the proposed medical service involves the use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer or any other type of therapeutic good, please provide the following details:

The proposed medical service, EGFR mutation testing, does not specify a particular methodology. Any appropriately accredited and validated EGFR mutation test methodology is within the scope of this application.

Australian molecular pathology service providers currently use a number of different commercial test kits and locally developed methods, the most common of which are the cobas® EGFR mutation test kit (v1 and v2), Therascreen®, Sequenom MassArray® and Sanger sequencing.

(b) Is the medical device classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

☒ Class III
☐ AIMD
☐ N/A

15. (a) Is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

☐ Yes (If yes, please provide supporting documentation as an attachment to this application form)
☒ No

(b) If no, has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

☒ Yes (if yes, please provide details below)
☐ No

The cobas® EGFR mutation test kit (v2) was used to determine EGFR mutation status in the osimertinib clinical development program.

ARTG listing, registration or inclusion number: 194319
TGA approved indication(s), if applicable: non-small cell lung cancer
TGA approved purpose(s), if applicable: Intended for the qualitative detection and identification of mutations in exons 18, 19, 20, and 21 of the EGFR gene in DNA derived from formalin-fixed paraffin-embedded tumour tissue or plasma from NSCLC patients. The test can be used as an aid in selecting patients with NSCLC for therapy with an EGFR TKI.

16. If the therapeutic good has not been listed, registered or included in the ARTG, is the therapeutic good in the process of being considered for inclusion by the TGA?

☐ Yes (please provide details below)
☐ No

Date of submission to TGA: Insert date of submission here
Estimated date by which TGA approval can be expected: Insert estimated date here
TGA Application ID: Insert TGA Application ID here
TGA approved indication(s), if applicable: If applicable, insert description of TGA approved indication(s) here
TGA approved purpose(s), if applicable: If applicable, insert description of TGA approved purpose(s) here

17. If the therapeutic good is not in the process of being considered for listing, registration or inclusion by the TGA, is an application to the TGA being prepared?

☐ Yes (please provide details below)

☐ No

Estimated date of submission to TGA: Insert date of submission here
Proposed indication(s), if applicable: If applicable, insert description of proposed indication(s)
Proposed purpose(s), if applicable: If applicable, insert description of proposed purpose(s) here

PART 4 – SUMMARY OF EVIDENCE

18. **Provide an overview of all key journal articles or research published in the public domain related to the proposed service that is for your application (limiting these to the English language only).** ***Please do not attach full text articles, this is just intended to be a summary.***

	Type of study design*	**Title of journal article or research project (including any trial identifier or study lead if relevant)**	**Short description of research (max 50 words)****	**Website link to journal article or research (if available)**	**Date of publication*****
1.	Phase III, randomised control study	Osimertinib vs standard of care (SoC) EGFR-TKI as first-line therapy in patients (pts) with EGFRm advanced NSCLC: FLAURA **FLAURA, NCT02296125**	FLAURA is a Phase III, double-blind, randomised study assessing the efficacy and safety of osimertinib versus a standard of care EGFR TKI (gefitinib or erlotinib) in patients with locally advanced or metastatic EGFRm+ NSCLC	http://www.esmo.org/Conferences/ESMO-2017-Congress/Press-Media/Press-Releases/Osimertinib-Improves-Progression-free-Survival-in-Patients-with-EGFR-Mutated-Lung-Cancer	2017
2.	Phase I, open-label, dose-escalation and dose expansion study	Osimertinib As First-Line Treatment of EGFR Mutation–Positive Advanced Non–Small-Cell Lung Cancer **AURA1A/1B or AURA Phase I component, NCT01802632**	AURA1A/1B included two cohorts of treatment-naïve patients to examine clinical activity and safety of osimertinib as first-line treatment of EGFR-mutated advanced non–small-cell lung cancer (NSCLC)	http://ascopubs.org/doi/abs/10.1200/JCO.2017.74.7576	2017

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment, including providing the trial registration number to allow for tracking purposes.*

**** If the publication is a follow-up to an initial publication, please advise.*

19. Identify yet to be published research that may have results available in the near future that could be relevant in the consideration of your application by MSAC (limiting these to the English language only). ***Please do not attach full text articles, this is just intended to be a summary. N/A***

	Type of study design*	**Title of research (including any trial identifier if relevant)**	**Short description of research (max 50 words)****	**Website link to research (if available)**	**Date*****
1.	For yet to be published research that may have results relevant to your application, insert the type of study design in this column and columns below	For yet to be published research that may have results relevant to your application, insert the title of research (including any trial identifier if relevant) in this column and columns below	For yet to be published research that may have results relevant to your application, insert a short description of research (max 50 words) in this column and columns below	For yet to be published research that may have results relevant to your application, insert a website link to this research (if available) in this column and columns below	For yet to be published research that may have results relevant to your application, insert date in this column and columns below
2.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date
3.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date
4.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date
5.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date
6.	Insert study design	Insert title of research	Insert description	Insert website link	Insert date

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment.*

****Date of when results will be made available (to the best of your knowledge).*

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

20. List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the service (please attach a statement of clinical relevance from each group nominated):

The Royal College of Pathologists of Australasia

The Medical Oncology Group of Australia

A letter of support has not been requested from the above organisations due to the routine nature of the EGFR mutation test in Australian practice. Support for EGFR mutation testing can be presumed from the existing QAP administered through RCPA on an ongoing basis.

21. List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):

As EGFR mutation testing is already available in the Australian health care system for the proposed population (MBS item number 73337), there is no appropriate comparator.

22. List the relevant consumer organisations relevant to the proposed medical service (please attach a letter of support for each consumer organisation nominated):

23. List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:

N/A

24. Nominate two experts who could be approached about the proposed medical service and the current clinical management of the service(s):

Name of expert 1:

Redacted
Redacted
Redacted
Redacted

Name of expert 2:

Redacted
Redacted
Redacted
Redacted

Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INDICATION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

25. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease in terms of both morbidity and mortality:

Lung cancer is the second-leading cause of premature death for all Australians. It is the fifth most commonly diagnosed cancer in Australia and the most common cause of cancer-related death.[1] The Australian Institute of Health and Welfare (AIHW) projects that in 2017, 12,434 Australians will be diagnosed with lung cancer. Of these patients, only 16% will remain alive in five years.[1] This poor survival rate is due in part to late presentation and detection, with over 50% of patients with lung cancer being diagnosed when the disease is already at an advanced and inoperable stage.[7] The risk of developing lung cancer increases with age and male gender. The average age at diagnosis in Australia is 71 years.[1]

Non-small cell lung cancer accounts for over 80% of all lung cancer cases and is divided into two major subtypes: non-squamous carcinoma (including adenocarcinoma, large-cell carcinoma and other cell types) and squamous cell (epidermoid) carcinoma.[2]

Regardless of histology, NSCLC arises as a consequence of either acquired and/or inherited mutations within the lung tissue. Over time such mutations lead to an abundance of abnormal cellular proteins and enzymes, disrupting physiological function, migration, proliferation and survival.

In approximately 15% of Australian patients with locally advanced or metastatic NSCLC, the disease is characterised by the presence of an EGFR gene mutation that is known to confer sensitivity to an EGFR TKIs (osimertinib, gefitinib, erlotinib).[3] Selective inhibition of EGFR tyrosine kinase has demonstrated clinical benefit in approximately 70% of patients with advanced NSCLC harbouring the EGFR sensitising mutations. The tumours initially respond to first and second generation EGFR-TKIs used currently (gefitinib and erlotinib), but subsequently develop resistance to therapy, with a median time to progression of nine months.[4-6] The most common underlying reason for EGFR TKI treatment failure is acquired resistance due to the development of a secondary EGFR *T790M* mutation.[8] It is proposed that treatment with osimertinib prolongs the time to development of this resistance, increasing survival and quality of life.

26. Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed medical service, including any details of how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the service:

In the Australian clinical setting, the majority of advanced/metastatic NSCLC patients will be under the care of a Medical Oncologist, will undergo mutation testing (at diagnosis) for the presence of an EGFR sensitising mutation or rearrangement of anaplastic lymphoma kinase (ALK) genes. EGFR status is stable over the course of the disease therefore testing occurs reflexively as part of the diagnostic work up. Request for EGFR mutation testing can come from a Medical Oncologist, Surgeon or Pathologist.

EGFR is a cellular transmembrane receptor found on the surface of cells. Activation of the EGFR occurs when specific ligands, including EGF or other growth factors, bind to the extracellular domain. This stimulates intracellular tyrosine kinase activity and a cascade of intracellular reactions leading to DNA synthesis and cell proliferation. Mutations of the EGFR gene may cause the gene to be constitutively "active" resulting in overexpression or activity and contributing to the development of cancers through tumour cell proliferation. Around 90% of all activating mutations are accounted for by exon 19 deletions or a point mutation in exon 21 (L858R).[9]

27. Define and summarise the current clinical management pathway *before* patients would be eligible for the proposed medical service (supplement this summary with an easy to follow flowchart [as

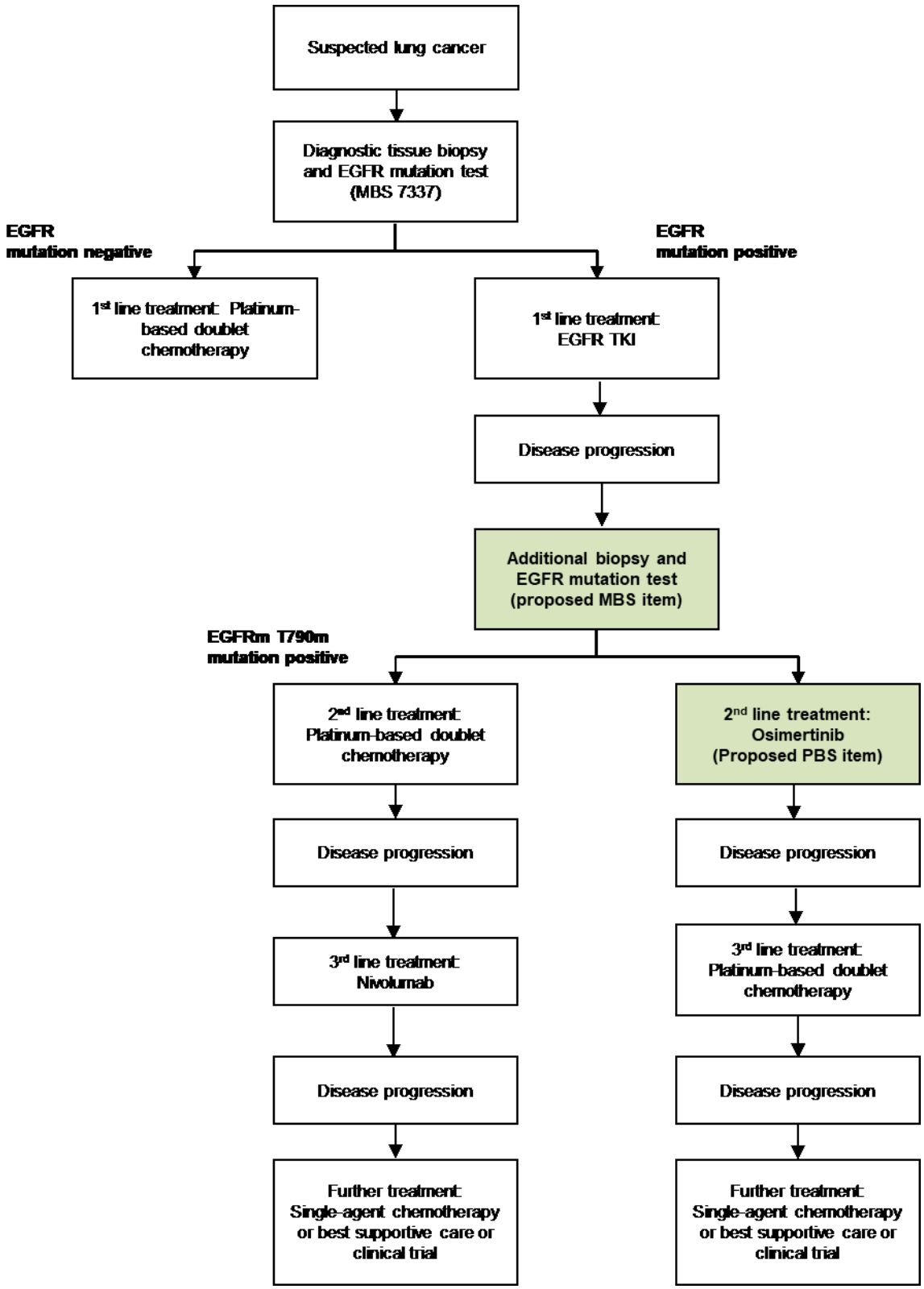
an attachment to the Application Form] depicting the current clinical management pathway up to this point):

The current clinical management pathway, based on Australian and international guidelines,[2, 10, 11] is presented in Figure 1. The proposed medical service, EGFR mutation testing for advanced NSCLC, is already available and publicly funded in Australia. Patients who are EGFR mutation positive following the testing are recommended the current standard of care EGFR TKIs, gefitinib or erlotinib.

The current MSAC application is part of a co-dependant submission that requests patients who are EGFR sensitising mutation positive are eligible for subsidised access to osimertinib in the first-line setting.

The boxes shaded green in Figure 1 refer to a separate co-dependent submission for an additional EGFR T790M mutation test and access to subsidised osimertinib in the second-line setting (Application number 1407). The current MSAC application is independent to Application number 1407 as they cover different proposed patient populations.

Figure 1 Current clinical management pathway in NSCLC



Note:
EGFR mutation negative population also includes ALK mutation positive and EGFR/ALK negative patients. This population has been excluded for non-relevance to the current application.
The boxes shaded green refer to a current co-dependent submission for an additional EGFR mutation test and osimertinib in the second-line for eligible patients (Application number 1407). The current MSAC application is independent to Application number 1407 as they cover different proposed patient populations.

PART 6b – INFORMATION ABOUT THE INTERVENTION

28. Describe the key components and clinical steps involved in delivering the proposed medical service:

In patients with NSCLC, EGFR mutation testing is well established as part of the diagnosis and classification pathway. Testing for EGFR gene mutation in patients with locally advanced or metastatic NSCLC involves:

(i) Sample collection: The two methods commonly used in Australia for tumour sampling for EGFR gene mutation testing are (i) bronchoscopy and (ii) percutaneous fine needle aspiration (FNA). Bronchoscopy is usually carried out by a respiratory physician and is the preferred method for sample collection as a greater cell mass can usually be obtained. When bronchoscopy is not possible FNA is the method used, usually carried out by radiologists, and is guided by computed tomography.

(ii) Preparation of the tissue sample: Qualified pathology department personnel will undertake preparation of biopsy material, i.e., chemical fixation, slicing, staining and mounting onto glass slides. Interpretation of histopathology and selection of biopsy samples or section slices containing appropriate cells for EGFR mutational analysis is performed by pathologists. Tumour samples collected at time of diagnosis/surgery are typically stored by the pathology department of the hospital where the diagnosis/surgery was undertaken. When a request to test for the presence of mutations in the EGFR gene is made by the treating physician, preparation and packaging of pathology samples or slides for dispatch to an accredited centre that conducts EGFR gene mutation testing is undertaken by pathology department administrative staff.

(iii) Testing the prepared sample for an activating mutation of the EGFR gene: If not prepared prior to being sent to the EGFR gene mutation testing laboratory, formalin-fixed, paraffin-embedded (FFPE) tissue blocks will be processed into sections and presented onto glass slides by qualified molecular pathology clinical scientists. An initial review of these slides is performed by a pathologist at the testing centre to determine sample quality and likelihood of yielding sufficient cancer cells required for analysis. If tumour cells of appropriate quality and quantity are identified, these are dissected from the pathology slide(s) by the pathologist. These cells are then processed in terms of their DNA extraction, followed by the amplification of DNA from candidate exons by qualified molecular pathology clinical scientists. These DNA samples are then analysed via validated platforms (e.g., direct gene sequencing) for the presence of EGFR mutations by qualified molecular pathology clinical scientists.

Process review, interpretation and reporting of results of the EGFR gene mutation test are performed by qualified senior molecular pathology clinical scientists and/ or qualified molecular pathologists and reported to the referring doctor.

29. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

Australian molecular pathology service providers currently use a number of different commercial test kits, the most common of which are the cobas® EGFR mutation test kit (Roche Molecular Systems, Inc.), Therascreen® (Qiagen NV) and Sequenom MassArray® (Sequenom Inc.).

30. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

N/A

31. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency):

32. If applicable, identify any healthcare resources or other medical services that would need to be delivered <u>at the same time</u> as the proposed medical service:

N/A

33. If applicable, advise which health professionals will primarily deliver the proposed service:

EGFR mutation testing is currently performed, and the results interpreted and reported by qualified pathologists.

34. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

N/A

35. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

N/A

36. If applicable, advise what type of training or qualifications would be required to perform the proposed service as well as any accreditation requirements to support service delivery:

The proposed service will be performed in pathology laboratories by qualified and registered personnel. All laboratories performing this service are accredited to the Royal College of Pathologist of Australasia Quality Assurance Programs.

37. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select all relevant settings):

☐ Inpatient private hospital
☐ Inpatient public hospital
☐ Outpatient clinic
☐ Emergency Department
☐ Consulting rooms
☐ Day surgery centre
☐ Residential aged care facility
☐ Patient's home
☒ Laboratory
☐ Other – please specify below

Specify further details here

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

Describe rationale here

38. Is the proposed medical service intended to be entirely rendered in Australia?

☒ Yes
☐ No – please specify below

Specify further details here

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

39. 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 (including identifying health care resources that are needed to be delivered at the same time as the comparator service):

EGFR mutation testing is already available in the Australian health care system for the proposed population (MBS item number 73337). This application requests an amendment to allow access to subsidised osimertinib for eligible patients.

For the co-dependent pair, the comparator is EGFR mutation testing followed by treatment with a first-generation EGFR TKI (erlotinib or gefitinib)

40. Does the medical service that has been nominated as the comparator have an existing MBS item number(s)?

☐ Yes (please provide all relevant MBS item numbers below)
☐ No

N/A

41. Define and summarise the current clinical management pathways that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards including health care resources):

Refer to Question 37 above.

42. (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)?

☐ Yes
☐ No

(b) If yes, please outline the extent of which the current service/comparator is expected to be substituted:

N/A

43. Define and summarise how current clinical management pathways (from the point of service delivery onwards) are expected to change as a consequence of introducing the proposed medical service including variation in health care resources (Refer to Question 39 as baseline):

Following the introduction of the proposed medical service, treatment naïve patients with locally advanced or metastatic EGFRm NSCLC will be eligible for treatment with subsidised osimertinib. Clinical evidence to be presented in the co-dependent submission shows the superiority of osimertinib compared to standard of care EGFR TKIs. Osimertinib is expected to be the new standard of care for the first-line treatment of EGFRm advanced NSCLC.

PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

44. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

For patients with treatment naïve locally advanced or metastatic EGFRm NSCLC, EGFR mutation testing followed by treatment with osimertinib is superior in terms of comparative effectiveness and non-inferior in terms of comparative safety, to EGFR mutation testing followed by treatment with standard of care EGFR TKIs (gefitinib or erlotinib).

45. Please advise if the overall clinical claim is for:

☒ Superiority
☐ Non-inferiority

46. Below, list the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be specifically measured in assessing the clinical claim of the proposed medical service versus the comparator:

Safety Outcomes:

Safety and tolerability of osimertinib treatment (adverse events assessed by CTCAE v4.0; clinical chemistry, hematology, and urinalysis; vital signs, physical examination, body weight; digital electrocardiogram; lefet ventricular ejection fraction; World Health Organisation performance status; ophthalmological assessment

Clinical Effectiveness Outcomes:

Progression free survival, objective response rate, duration of response, overall survival

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

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

EGFR mutation testing is proposed to determine eligibility for access to osimertinib in treatment naïve patients with locally advanced or metastatic EGFRm NSCLC.

The Australian Institute of Health and Welfare (AIHW) have projected the incidence of lung cancer in Australia in 2019 to be 13270. The best estimate of the population to be tested for EGFR mutation and be eligible for EGFR TKI including osimertinib is presented in Table 1.

Table 1 Estimated eligible population in 2019

Projected incidence lung cancer in 2019	13,270
Proportion of patients with NSCLC[7]	64%
Proportion of patients with Stage IIIb/IV[7]	59%
Proportion of patients with EGFRm[3]	15%

48. Estimate the number of times the proposed medical service(s) would be delivered to a patient per year:

EGFR mutation testing is currently delivered once to a patient to determine their eligibility for first-line EGFR TKIs. It is still proposed that one lifetime reflex EGFR mutation test is required per patient. There will be no increase in the number of tests or cost to the MBS as a result of the amended listing.

49. How many years would the proposed medical service(s) be required for the patient?

Only one lifetime reflex EGFR mutation test is required per patient.

50. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

The projected number of patients who will utilise EFGR mutation testing for the first full year (projected to be 2019) is 5011, as calculated in Table 2. It is estimated that 752 patients will be EGFR mutation positive and be eligible for first-line EGFR TKI including osimertinib.

Table 2 Projected number of patients to utilise EGFR mutation testing in Year 1

Projected incidence lung cancer in 2019	13,270
Proportion of patients with NSCLC (64% of 13270)	8493
Proportion of patients with Stage IIIb/IV (59% of 8493)	5011
Proportion of patients with EGFRm	752

51. Estimate the anticipated uptake of the proposed medical service over the next three years factoring in any constraints in the health system in meeting the needs of the proposed population

(such as supply and demand factors) as well as provide commentary on risk of 'leakage' to populations not targeted by the service:

It is anticipated that all newly eligible patients, i.e. locally advanced or metastatic NSCLC patients, over the next three years will undertake the proposed medical service. The number of patients estimated to utilise EGFR mutation testing over the next three years in presented in Table 3. The risk of leakage is anticipated to be minimal. As EGFR testing is already a routine step in the diagnosis and classification of lung cancer, there will be no increase in the number of tests performed or cost to the MBS as a result of this application.

Table 3 Projected uptake over the next three years

	2020	2021	2022
Projected incidence lung cancer	13640	14022	14415
Proportion of patients with NSCLC (64% of 13270)	8730	8974	9226
Proportion of patients with Stage IIIb/IV (59% of 8493)	5151	5295	5443

PART 8 – COST INFORMATION

52. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

The current cost of EGFR mutation test (MBS item #73337) is $307.35 per test. This figure is not anticipated to change with the addition of eligibility for osimertinib for patients with EGFR mutation.

53. Specify how long the proposed medical service typically takes to perform:

For a standard EGFR mutation test, the time taken in a laboratory to perform the test is shown below.

- Sanger Sequencing – 24-48 hrs Companion diagnostics (Qiagen Pyrosequencing & Roche cobas); average of 3 to 5 days
- NGS (Ion Torrent & Illumina) 5-7 Days

54. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and medical service usage characteristics that would define eligibility for MBS funding.

Category 6 – Pathology services
Proposed item descriptor: A test of tumour tissue from a patient diagnosed with non-small cell lung cancer, shown to have non-squamous histology or histology not otherwise specified, requested by, or on behalf of, a specialist or consultant physician, to determine if the requirements relating to epidermal growth factor receptor (EGFR) gene status for access to erlotinib, gefitinib or **osimertinib** under the Pharmaceutical Benefits Scheme (PBS) are fulfilled Fee: $397.35

PART 9 – FEEDBACK

The Department is interested in your feedback.

55. How long did it take to complete the Application Form?

Insert approximate duration here

56. (a) Was the Application Form clear and easy to complete?

☐ Yes
☐ No

(b) If no, provide areas of concern:

Describe areas of concern here

57. (a) Are the associated Guidelines to the Application Form useful?

☐ Yes
☐ No

(b) If no, what areas did you find not to be useful?

Insert feedback here

58. (a) Is there any information that the Department should consider in the future relating to the questions within the Application Form that is not contained in the Application Form?

☐ Yes
☐ No

(b) If yes, please advise:

Insert feedback here

References

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8. Chong, C.R. and P.A. Janne, *The quest to overcome resistance to EGFR-targeted therapies in cancer.* Nat Med, 2013. **19**(11): p. 1389-400.
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10. Novello, S., et al., *Metastatic non-small-cell lung cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.* Ann Oncol, 2016. **27**(suppl 5): p. v1-v27.
11. Cancer Council Australia Lung Cancer Guidelines Working Party. *Clinical practice guidelines for the treatment of lung cancer* http://wiki.cancer.org.au/australia/Guidelines:Lung_cancer. 2017 9 Oct 2017]; Available from: http://wiki.cancer.org.au/australia/Guidelines:Lung_cancer.