Australian Government

Department of Health

Consultation Survey on MSAC Application 1721

Small gene panel testing for non-small cell lung carcinoma

MSAC welcomes feedback on MSAC applications for public funding from individuals, organisations representing health professionals or consumers and/or carers, and from other stakeholders. Please use this template to prepare your feedback. You may also attach additional information if you consider it may be useful in informing MSAC and its sub-committees.

Sharing consultation feedback

Submitted consultation feedback will be shared with the Applicant and with MSAC and its sub-committees.

- The applicant will receive a summary of comments from individuals, with the individual's name and other identifying information removed.
- MSAC and its sub-committees will receive both the summary and copies of the comments, with the name of the individual and other identifying information removed.
- Consultation feedback from groups or organisations will be provided in a complete form to both the Applicant and to MSAC and its sub-committees.

Please do not include information in your feedback that you do not want shared as outlined above. In addition, to protect privacy, do not include identifying personal (e.g. name) or sensitive (e.g. medical history) information about third parties, such as medical professionals or friends/relatives.

How consultation feedback is used

MSAC and its sub-committees consider consultation feedback when appraising an application, including to better understand the potential impact of the proposed medical technology/service on consumers, carers, and health professionals. A summary of consultation feedback will be included in the Public Summary Document (PSD) published on the MSAC website once MSAC has completed its appraisal. The PSD may also cite feedback from groups/organisations, including the name of the organisation. As such, organisations should not include information or opinions in their feedback that they would not wish to see in the public domain.

Consultation deadlines. Please ensure that feedback is submitted by the pre-PASC or pre-MSAC consultation deadline for this application. Consultation deadlines for each PASC and MSAC meeting are listed in the PASC and MSAC and ESC calendars available on the MSAC website. They are also published in the MSAC Bulletin. Feedback received after the respective deadlines may not be considered.

For further information on the MSAC consultation process please refer to the MSAC Website or contact the Consumer Evidence and Engagement Unit on email: commentsMSAC@health.gov.au.
Thank you for taking the time to provide your feedback. Please return your completed survey to:

Email: commentsMSAC@health.gov.au

Mail: MSAC Secretariat,
MDP 960, GPO Box 9848,
ACT 2601

PART 1 – PERSONAL AND ORGANISATIONAL INFORMATION

1. Respondent details

Name: Matilda Haas

Email: matilda.haas@mcri.edu.au

Phone No: 0399366345

2. Is the feedback being provided on an individual basis or by a collective group?

☐ Individual
☒ Collective Group

If an individual, specify the name of the organisation you work for

If a collective group, specify the name of the group

Australian Genomics Health Alliance (Australian Genomics), including specific expertise and experience from collaborators.

3. How would you best identify yourself?

☐ General Practitioner
☐ Consumer
☐ Care giver
☒ Other

If other, please specify

Australian Genomics, in consultation with senior program administrators, clinicians, researchers and community representatives from Australian Genomics.

PART 2 – CLINICAL NEED AND PUBLIC HEALTH SIGNIFICANCE

4. Describe your experience with the medical condition (disease) and/or proposed intervention and/or service relating to the application form

Australian Genomics is an Australian Government initiative supporting genomic research and its translation into clinical practice. Through broad engagement and a national collaborative approach, it achieves two key objectives: to improve efficiency, reach and timeliness of genomic research projects, and to support Commonwealth, State and Territory health departments in the implementation of genomics research outcomes by refining and communicating evidence to inform policy development.

Australian Genomics engages with current and emerging government policy and priorities to identify gaps and opportunities, to support policy and action for integrating genomic technologies into the health system. By interfacing with consumers, government, industry and global genomics initiatives, Australian Genomics drives change and growth in the sector.

Australian Genomics has investigated clinical implementation of genomic testing into a range of rare disease and cancer diseases. This had included a Somatic flagship, that investigated clinically actionable variants in a range of cancer types using the Comprehensive Cancer Panel (391 cancer gene panel) at the Peter MacCallum Cancer Centre. This study, on unresectable solid tumours (including non-small cell lung cancer (NSCLC)) also investigated the implementation of treatment changes in patients after their genomic result.

An Australian Genomics Lung Cancer Diagnosis flagship has investigated the methodology of endobronchial ultrasound lymph node aspirates for nucleotide extraction and whole genome / whole exome sequencing technologies, to guide lung cancer treatment.

Australian Genomics also engages a Community Advisory Group which includes members who have personal experience with genetic conditions including cancer.

5. What do you see as the benefit(s) of the proposed medical service, in particular for the person involved and/or their family and carers?

The Application 1721 will allow for faster and more comprehensive genomic testing, for detection of targetable mutations and better and faster treatment decision making. This will lead to better health outcomes and affect quality of life and outcome for patients.

The genomic testing process, including cost and time to result will be more efficient. This is particularly important in NSCLC, given that up to 75% of patients present at an advanced stage and do not undergo surgery (Melosky et al., 2018). Tissue samples are usually taken via fine-needle aspirations of primary or metastatic sites.

Another advantage, therefore, is that one biopsy is used for a more comprehensive test, reducing the potential discomfort associated with re-biopsy, as well as maximising the value of the sample. Simultaneous testing also provides the person with a more straightforward diagnostic pathway to understand at a time where they may be under considerable distress. In rare circumstances where a person has more than one genetic mutation, this will also be more likely diagnosed through the proposed NGS test.

Additional benefits to the health system include ensuring that patients don't receive treatments they don't need and which may be clinically harmful to the patient.

6. What do you see as the disadvantage(s) of the proposed medical service, in particular for the person involved and/or their family and carers?

There is no disadvantage to the person or their family and carers compared to the current service of sequential testing. The proposed service will provide faster and more complete testing that will avoid patients missing out on best treatment possible.

7. What other benefits can you see from having this intervention publically funded?

Public funding would allow patients to receive the best treatment possible, avoiding futile expensive treatments which waste funds. It also reduces the chance of being prescribed a wrong, potentially detrimental treatment, or one that has less chance of providing social benefit to the population.

By being publically funded, it is more likely that the NGS test will make the most efficient use of scarce tumour tissue, in order to inform clinical management.

8. What other services do you believe need to be delivered before or after this intervention, eg Dietician, Pathology etc?

Genome scientists to curate the genomic variants and a molecular tumour board (multidisciplinary team including physicians, oncologists, surgeons, radiologists, pathologists, genomic scientists and researchers) to discuss the treatment plan based on genomic findings.

Genetic counselling services are not usually required for tumour testing as proposed, as germline variants are not identified.

PART 3 – INDICATION(S) FOR THE PROPOSED MEDICAL SERVICE AND CLINICAL CLAIM

9. Do you agree or disagree with the proposed population(s) for the proposed medical service as specified in Part 6a of the application form?

- [x] Strongly Agree
- [ ] Agree
- [ ] Disagree
- [ ] Strongly Disagree

Specify why or why not:

A single test for multiple targets will positively impact lung cancer patients.

10. Have all the associated interventions been adequately captured in Part 6b of the application form?

- [x] Yes
- [ ] No

Please explain:

11. Do you agree or disagree that the comparator(s) to the proposed medical service as specified in Part 6c of the application form?

- [x] Strongly Agree
- [ ] Agree
- [ ] Disagree
- [ ] Strongly Disagree

Please explain:

The current sequential molecular tests are correctly described. The current issue is that the majority of patients have insufficient tissue for all the tests and for the majority they are not fully tested for all potential targetable mutations that have available treatments. This leads to less than ideal treatment options that are not selected on the basis of fully informed test results.

12. Do you agree or disagree with the clinical claim made for the proposed medical service as specified in Part 6d of the application form?

- [x] Strongly Agree
- [ ] Agree
- [ ] Disagree
- [ ] Strongly Disagree

Specify why or why not:

Reduction of the number of patients required to be subjected to new biopsy is both economically and socially efficient. The majority of lung cancer patients present with advanced disease that urgently require decisive, targeted therapy to stem their rapid clinical decline and to alleviate their debilitating symptoms.

PART 4 – COST INFORMATION FOR THE PROPOSED MEDICAL SERVICE

13. **Do you agree with the proposed service descriptor?** MSAC is transitioning to new application forms so the relevant question in the application form will vary depending on the version used. For medical services on the MBS, see question 51 or 53. For medical services seeking funding from a source other than the MBS, see question 52 (new application forms only—labelled v. 2.5).

☒ Strongly Agree
☐ Agree
☐ Disagree
☐ Strongly Disagree

Specify why or why not:

From the information shown the application, sequential testing would be cheaper for EGFR, compared to a panel approach. However, it would be more expensive by the time you add in testing for ROS1, and NGS with a small panel will be faster and overall less expensive when assessing all possible variants listed. As outlined in the application, a small NGS panel takes less time for assessment and reporting compared to sequential testing (10 vs 13.5 days) (Dall'Olio et al., 2020).

The wording for the small panel test in (i) and (ii) refer to "at least" testing for the genes listed. This is a good approach given that more genes could be incorporated into the panel test over time.

The application outlines two service descriptors, which are based on two potential approaches to the testing depending on "each individual laboratories capabilities and infrastructure". The merits of the two-step test versus the one-step test should be further explored, so as not to set up any inequity of access issues in relation to accessing the best available testing approaches. The applicants state that "as there are advantages and disadvantages with the both approaches, the College would welcome a discussion with the Department as to whether it is feasible to list both, or just one approach". We strongly urge the Department to explore this further with the College and expert stakeholders.

14. **Do you agree with the proposed service fee?** MSAC is transitioning to new application forms, so the relevant question in the application form will vary depending on the version used. For medical services on the MBS, see question 51 or 53. For medical services seeking funding from a source other than the MBS, see question 52 (new application forms only—labelled v. 2.5).

☒ Strongly Agree
☐ Agree
☐ Disagree
☐ Strongly Disagree

Specify why or why not:

The current combined testing for single gene variants for EGFR (73337); IHC (72846); FISH for ALK status for access to drug (73341); FISH for ROS for access to drug (73344); EGFR gene status for access to drug (73351) combine to a total cost over $1600. While we fully understand that it is potentially unlikely that most people with NSCLC in Australia would progress through all of the tests due to drop out at each step, this should be considered in comparison with the more comprehensive, faster turnaround and less patient burdensome NGS test which is priced at a fee of $1247. Furthermore, studies have shown that one NGS test is more cost-effective than stepwise testing even when drop out is included in the model (Dall'Olio et al., 2020). The fee for this proposed

test could also be considered in the context of another MSAC application, 1669 KRAS G12C variant testing for access to sotosasib which was assigned a fee of $397.35 for a single gene test to assess treatment suitability.

PART 5 – ADDITIONAL COMMENTS

15. Do you have any additional comments on the proposed intervention and/or medical condition (disease) relating to the proposed medical service?

The US NCCN guidelines (March, 2021) recommend an NGS based test with simultaneous analysis of ALK rearrangements, BFAF mutations, EGFR mutations, METex14 skipping mutations, NTRK1/2/3 gene fusions, RET rearrangements and ROS1 rearrangements. Additionally, that the status of these genes should be known before deciding whether to use targeted therapy or immunotherapy with or without chemotherapy (Ettinger et al., 2021).

ESMO Europe recommends NGS multi-gene panels (Mosele et al., 2020), whilst also acknowledging the health economic issue of NGS tests results indicating drug selection outside of their approved indications. Notably, Yu (et al., 2018) also found that decreasing tests costs were associated with increased treatment costs.

This application for expanded, single time point testing for Australian patients will align well with current standards of patient care in Canadian and UK health systems. Canadian guidelines have similar molecular targets for NSCLC (recommended EGFR, ALK and ROS1 rearrangement, BRAF V600 testing at diagnosis) (Melosky et al., 2020). The UK National genomic test directory for cancer has a multi-target NGC panel – small variant (M4.1: EGFR, QLK, BRAF, KRAS p.(G12C), MET exon 14 skipping) and also a mult-target NGS panel – structural variant (M4.2: ROS1, RET, EML4-ALK, NTRK1, NTRK2, NTRK3, MET 14 exon skipping).

Melosky et al., (2020) also noted the need for protein expression level testing of PD-L1; ERBB2 Exon 20 insertion and TP53 variants. It is important to continue to review the gene panel list to facilitate incorporation of novel genes / biomarkers as advances are made.

16. Do you have any comments on this feedback survey? Please provide comments or suggestions on how this process could be improved.

Again, thank you for taking the time to provide valuable feedback.

References

Dall'Olio, F. G., N. Conci, G. Rossi, M. Fiorentino, A. De Giglio, G. Grilli, A. Altimari, E. Gruppioni, D. M Filippini, A. Di Federico, G. Nuvola, and A. Ardizzoni. 2020. 'Comparison of Sequential Testing and Next Generation Sequencing in advanced Lung Adenocarcinoma patients - A single centre experience', *Lung Cancer*, 149: 5-9.

Ettinger, D. S., D. E. Wood, D. L. Aisner, W. Akerley, J. R. Bauman, A. Bharat, D. S. Bruno, J. Y. Chang, L. R. Chirieac, T. A. D'Amico, T. J. Dilling, J. Dowell, S. Gettinger, M. A. Gubens, A. Hegde, M. Hennon, R. P. Lackner, M. Lanuti, T. A. Leal, J. Lin, B. W. Loo, Jr., C. M. Lovly, R. G. Martins, E. Massarelli, D. Morgensztern, T. Ng, G. A. Otterson, S. P. Patel, G. J. Riely, S. E. Schild, T. A. Shapiro, A. P. Singh, J. Stevenson, A. Tam, J. Yanagawa, S. C. Yang, K. M. Gregory, and M. Hughes. 2021. 'NCCN Guidelines Insights: Non-Small Cell Lung Cancer, Version 2.2021', *J Natl Compr Canc Netw*, 19: 254-66.

Melosky, B., N. Blais, P. Cheema, C. Couture, R. Juergens, S. Kamel-Reid, M. S. Tsao, P. Wheatley-Price, Z. Xu, and D. N. Ionescu. 2018. 'Standardizing biomarker testing for Canadian patients with advanced lung cancer', *Curr Oncol*, 25: 73-82.

Mosele, F., J. Remon, J. Mateo, C. B. Westphalen, F. Barlesi, M. P. Lolkema, N. Normanno, A. Scarpa, M. Robson, F. Meric-Bernstam, N. Wagle, A. Stenzinger, J. Bonastre, A. Bayle, S. Michiels, I. Bieche, E. Rouleau, S. Jezdic, J. Y. Douillard, J. S. Reis-Filho, R. Dienstmann, and F. Andre. 2020. 'Recommendations for the use of next-generation sequencing (NGS) for patients with metastatic cancers: a report from the ESMO Precision Medicine Working Group', *Ann Oncol*, 31: 1491-505.

Yu, T. M., C. Morrison, E. J. Gold, A. Tradonsky, and R. J. G. Arnold. 2018. 'Budget Impact of Next-Generation Sequencing for Molecular Assessment of Advanced Non-Small Cell Lung Cancer', *Value Health*, 21: 1278-85.