Australian Government

Department of Health

Consultation Survey on MSAC Application 1658

Testing of tumour tissue to determine a positive homologous recombination deficiency status in women newly diagnosed with advanced (FIGO stage III-IV) high grade epithelial ovarian, fallopian tube or primary peritoneal cancer, for access to PBS olaparib

This feedback survey relates to the application form and Population, Intervention, Comparator and Outcome (PICO) Confirmation for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)).

Please use this template, to prepare your feedback on the application form and/or the PICO Confirmation. You are welcome to provide feedback from either a personal or group perspective for consideration by the Department of Health when the application is being reviewed.

The data collected will be used to inform the Medical Services Advisory Committee (MSAC) process to ensure that when proposed healthcare interventions are assessed for public funding in Australia, they are patient focused and seek to achieve best value.

This feedback survey should take approximately 15 minutes to complete.

You may also wish to supplement your responses with further documentation or diagrams or other information to assist the Department in considering your feedback.

Thank you for taking the time to provide valuable feedback.

Responses may be provided to the MSAC, its subcommittees, a health technology assessment group and the applicant. Should you require de-identification please contact the HTA team (details below).

While stakeholder feedback is used to inform the application process, you should be aware that your feedback may be used more broadly by the applicant.

Please reply to the HTA Team:

Email: HTA@health.gov.au

Postal: MDP 959 GPO 9848 ACT 2601

PART 1 – PERSONAL AND ORGANISATIONAL INFORMATION

1. Respondent details

Name: Dr Matilda Haas

Email: matilda.haas@mcri.edu.au

Phone No: 0403287727

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

☐ Individual
☒ Collective Group

(b) If individual, specify the name of the organisation you work for

(c) If collective group, specify the name of the group

Australian Genomics

3. How would you best identify yourself?

☐ General Practitioner
☐ Specialist
☐ Researcher
☐ Consumer
☐ Care giver
☒ Other

(a) If other, please specify

Research Projects and Partnership Manager submitting a response on behalf of Australian Genomics in consultation with researchers and senior administration.
Please note this response has been prepared by generalist health and medical research professionals with experience in genetics/genomics and cancer research, but not in the specific area of oncology that is the subject of this application.

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, governments, 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 has 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 non-resectable solid tumours also investigated the implementation of treatment changes in patients after their genomic result.

Additionally, the Hereditary Cancer Syndromes flagship utilised whole genome sequencing to investigate causative variants in a range of familial cancers, providing additional treatment and management option for families. This work made use of the ICCon network of Familial Cancer Centres and researchers.

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?

People affected by these devastating cancers would welcome the opportunity to experience better outcomes afforded by personalised medicine approaches, in this instance through access to a new test that is a pre-requisite for access to another drug option. The application cites evidence that access to the drug extends the progression free survival period by months, and so warrants careful consideration.

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?

The evidence base for this test is complicated, not entirely supportive, and seems to be the subject of ongoing controversy in oncology (Pellegrino et al., 2019). HRD is complex and dynamic in nature, and with several different types of test being developed, yet no functional assay, it can be difficult to interpret the current available evidence on utility, although recent recommendations cited in the application are available (eg Miller et al., 2020).

It is also not clearly stated in this version of the application what kind of test is being proposed here (ie what does the genomic instability test involve?). It may be based on the Myriad test for genomic scarring, which tests for the presence of loss of heterozygosity (LOH), telomeric allelic imbalance (TAI), and large-scale state transitions (LST) across the genome. If the test is approved but without clarity on the methodology, it does not give other providers the opportunity to develop similar tests, affecting accessibility, nor allow a competitive environment to improve upon the test. The application notes that there may be a period of 1-2 years where only the proposed testing service will offer the test in Australia – prior to either other commercially available kits, or the development of the test in other Australian diagnostic laboratories which

would have considerable risk of monopoly pricing, especially in the context of the REDACTED proposed cost.

The other limitation is that HRD testing is currently done only in the context of determining whether PARP inhibitors are going to be useful, which may indicate limited utility due to decreased applicability to other inhibitors of key targets of Homologous Recombination Repair (HRR).

There is also the question about developing resistance to PARP inhibitors, so overprescribing or mis-prescribing should be avoided, since it seems to be a powerful option when used in specific contexts.

In the absence of better available tests, MSAC needs to weigh up whether approving this test now will do more good than harm, while potentially in future there may be better, more accurate tests available.

However, it should be noted that the HRD as an indicator for PARP inhibitor use has been approved by the FDA and Pellegrino et. al., do surmise the current information to conclude that for ovarian cancer, HRR status can inform patients who will receive maximum benefit from PARP inhibitor maintenance after platinum therapy.

Pellegrino et al., 2019 doi:10.1136/esmoopen-2018-000480

Miller et al., 2020 https://doi.org/10.1016/j.annonc.2020.08.2102

7. What other benefits can you see from having this intervention publicly funded on the Medicare Benefits Schedule (MBS)?

Having this test publicly funded may promote continued development of HRD tests and locally run clinical trials to contribute to the evidence for this intervention and drug combination.

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

The involvement of pathology in retrieving the tumour sample is already noted in the application.

Given the interrelationship between somatic and germline BRCA testing and this proposed pathway, genetics services and genetic counselling should be involved and referred to as appropriate and considered as an important facilitator in explaining the test and its outcomes to patients.

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?

- ☐ Strongly Agree
- ☒ Agree
- ☐ Disagree
- ☐ Strongly Disagree

(a) Specify why or why not:

Some of the key trials on the efficacy of PARPi have been done in relapsed patients (reviewed by Pellegrino et al., 2019), should this intervention and therapy be considered for relapsed as well as newly diagnosed patients?

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

- ☐ Yes
- ☒ No

(b) Please explain:

It is not clear whether in this test HRD will be tested by screening germline or somatic HR repair genes, evaluating the genomic scar (loss of heterozygosity, telomeric allelic imbalance and large-scale state transitions), or all three? This information may be available in other application materials not reviewed by us, such as the summary dossier.

From a genetics perspective there is a concern about the focus on BRCA with this application (although it makes sense given the corresponding germline item number). In Figure 3, (referral pathways) – referral to genetics services would be warranted not only those who have a positive BRCA tumour test but also those whose tumours do have HRD, as it may be due to a germline mutation in another ovarian cancer predisposition gene. While these women should be captured anyway as national guidelines (eviQ) recommend BRCA germline testing for all women diagnosed with high-grade epithelial ovarian cancer at any age (and most would be offered BRCA testing as part of a gene panel), but the stringent referral pathway/model of care described in this application will result in women not being referred to genetic services and/or receiving germline testing.

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

- ☐ Strongly Agree
- ☒ Agree
- ☐ Disagree
- ☐ Strongly Disagree

No additional comments

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?

- ☐ Strongly Agree
- ☒ Agree
- ☐ Disagree
- ☐ Strongly Disagree

(a) Specify why or why not:

This claim is in line with the recent clinical trial data explained in the application (PAOLA-1/ENGOT-ov25 trial).
It would be advisable to access more information on current uncertainties and controversy in oncology about the usefulness of the HRD test, as it seems possible that the utility of this HRD test / olaparib combination is strengthened by the performance of the drug rather than the test in defining the population to receive it?

PART 4 – COST INFORMATION FOR THE PROPOSED MEDICAL SERVICE

13. Do you agree with the proposed MBS item descriptor, as specified in Question 53 of the application form?

- ☐ Strongly Agree
- ☒ Agree
- ☐ Disagree
- ☐ Strongly Disagree

(b) Specify why or why not:

This description sufficiently describes what the test is, but not the methodology used. Is it important to describe the sequential nature of testing? That is, if BRCA1/2mt is reported, progression to HRD testing is not done. It would seem important for medical professionals ordering this test to be aware of that given the range of testing options available to them.

14. Do you agree or disagree with the proposed MBS fee, as specified in Question 53 of the application form?

- ☐ Strongly Agree
- ☐ Agree
- ☐ Disagree
- ☐ Strongly Disagree

(c) Specify why or why not:

The proposed fee has been redacted so it is not possible to comment. The fee should be considered in the context that the current cost of the Myriad HRD test (US$4,040).

Also, if the BRCA1/2 test returns a positive result for a pathogenic or likely pathogenic variant, HRD testing is not done – therefore the cost of this test would have to be close to the current cost of the BRCA test alone ($1,000) otherwise it does not represent value for money. Or, if progression to HRD testing does not happen, does the test revert to a BRCA1/2 testing item number?

Again, it is unclear where panel testing for non-BRCA ovarian cancer susceptibility genes fit into this testing pathway.

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?

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.