



**Australian Government**

**Department of Health**

# **Application Form**

**(New and Amended Requests for Public Funding)**

(Version 2.5)

**PD-L1 (Programmed Death 1 Ligand)  
immunohistochemistry testing for access to  
pembrolizumab as first-line therapy for patients recurrent  
or metastatic head and neck squamous cell carcinoma  
(HNSCC)**

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.

Phone: +61 2 6289 7550

Fax: +61 2 6289 5540

Email: [hta@health.gov.au](mailto:hta@health.gov.au)

Website: [www.msac.gov.au](http://www.msac.gov.au)

# PART 1 – APPLICANT DETAILS

## 1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant):

Corporation name: Merck Sharp & Dohme (Australia) Pty Limited

ABN: 14 000 173 508

Business trading name: N/A

### Primary contact name: REDACTED

Primary contact numbers

Business: REDACTED

Mobile: REDACTED

Email: REDACTED

### Alternative contact name: REDACTED

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

PD-L1 (Programmed Death-Ligand 1) immunohistochemistry testing for access to pembrolizumab as first-line therapy for patients with recurrent or metastatic head and neck squamous cell carcinoma.

### 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)

Recurrent or metastatic (R/M) head and neck squamous cell carcinoma (HNSCC). Head and neck cancer includes tumours arising from the oral cavity, pharynx, larynx, nasal cavity, paranasal sinuses, thyroid and salivary glands. Individuals who have progressed following initial definitive treatment have recurrent disease and require subsequent treatment. Patient who present with metastatic disease generally receive the same therapy as those with recurrent disease following initial definitive treatment.

### 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)

Immunohistochemistry (IHC) test for evaluation of Programmed Cell Death-Ligand 1 (PD-L1) expression to determine eligibility for treatment with pembrolizumab in patients with R/M HNSCC. The biopsy sample taken as part of a standard diagnostic process will be used for immunohistochemical testing with PD-L1. The testing would be done by a pathologist alongside other immunohistochemical tests which are done routinely.

### 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:

Insert relevant MBS item numbers here

### (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

**(g) If yes, please advise:**

Insert description of other public funding mechanism here

**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

This application is being lodged to support a co-dependent technology submission for access to pembrolizumab in patients with R/M HNSCC who express PD-L1.

Pembrolizumab (Keytruda) is currently PBS listed for use in advanced malignant melanoma (10424P, 10436G, 10475H, 10493G).

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

Trade name: Keytruda

Generic name: Pembrolizumab

**12. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Protheses List?**

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?**

Single use consumables: PD-L1 is evaluated using the PD-L1 pharmDx kit.

Multi-use consumables:

## 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:**

Type of therapeutic good: The PD-L1 test is an in vitro diagnostic test.

Manufacturer's name: Dako Pty Limited/Agilent

Sponsor's name: Merck Sharp & Dohme (Australia) Pty Limited

- (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

- 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)

ARTG listing, registration or inclusion number: 282595

TGA approved indication(s), if applicable: NA

TGA approved purpose(s), if applicable:

For In Vitro Diagnostic Use

IVDs that are intended to be used in histology and cytology to provide information about the presence and localisation of specific proteins and antigens present in histological tissue sections, cytological smears and fluids

- 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.	Non-randomised	Pembrolizumab after progression on platinum and cetuximab in head and neck squamous cell carcinoma (HNSCC): results from KEYNOTE-055.	KEYNOTE-055 is an open-label phase 2 non-randomised study of pembrolizumab in patients with R/M HNSCC resistant to platinum and cetuximab therapies. A total of 171 patients received $\geq 1$ dose of pembrolizumab. At a median follow up of 4 months, the ORR was 15% with a median duration of response of 7 months.	<a href="https://academic.oup.com/annonc/article/2799694/Pembrolizumab">https://academic.oup.com/annonc/article/2799694/Pembrolizumab</a>	11 October 2016

\* 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.**

	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.	Randomized, active-controlled, multi-site, open-label phase 3 trial	A Phase 3 Clinical Trial of Pembrolizumab (MK-3475) in First Line Treatment of Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma  KEYNOTE-048	KEYNOTE-048 is a phase 3 randomized, active-controlled, multi-site, open-label three arm trial in a 1:1:1 ratio, comparing pembrolizumab alone to pembrolizumab in combination with a platinum-based drug (cisplatin or carboplatin) + 5-Fluorouracil (5-FU), and to cetuximab + a platinum-based drug (cisplatin or carboplatin) + 5-FU in patients with R/M HNSCC.  N = 825	<a href="https://clinicaltrials.gov/ct2/show/NCT02358031">https://clinicaltrials.gov/ct2/show/NCT02358031</a>	TBD

\* 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):**

RCPA – Royal College of Pathologists of Australasia

MOGA – Medical Oncology Group of Australia

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

MOGA and RCPA

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

TBC

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

N/A in Australia

- 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**

Telephone number(s): **REDACTED**

Email address: **REDACTED**

Justification of expertise **REDACTED**

Name of expert 2: **REDACTED**

Telephone number(s): **REDACTED**

Email address: **REDACTED**

Justification of expertise: **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:**

Head and neck cancer includes cancers from 18 different sites including those that occur in the oral cavity, pharynx, larynx, nasal cavity, paranasal sinuses, thyroid and salivary glands. It is not uncommon for patients to have multiple cancers in different sites of the head and neck. The human papillomavirus (HPV) as well as Epstein-Barr virus and cytomegalovirus have been associated with the incidence of head and neck cancers. Head and neck cancer is the fifth most common cancer worldwide, and accounts for 5% of all malignancies. In Australia, head and neck cancer was the 7<sup>th</sup> most commonly diagnosed cancer in Australia in 2013, with 4,409 new cases. In 2014, head and neck cancer was the 15<sup>th</sup> leading cause of cancer death in Australia. Between 2009-2013, individuals diagnosed with head and neck cancer had a 69% chance of surviving for 5 years as compared to the general Australian population.

A large number of patients with head and neck cancer initially present with locally advanced, Stage III/IV disease. Initial treatment involves combinations of chemotherapy/radiation and/or surgery, designated “definitive” therapy. This definitive treatment can result in disease control for between 33-86% of patients. Individuals who have progressed following initial definitive treatment have recurrent disease and require subsequent treatment. Patient who present with metastatic disease generally receive the same therapy as those with recurrent disease following initial definitive treatment.

**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:**

PD-L1 testing would be undertaken in patients diagnosed with R/M HNSCC. The anticipated indication will be for first line treatment in these patients. This application requests consideration of PD-L1 testing in order to access pembrolizumab monotherapy. However, KNO48 also has a combination therapy arm containing pembrolizumab together with a platinum based drug and 5-FU. Although the combination arm is expected to work in all patients, this application wishes to apply testing to these patients, in the event that the data supports testing. Males account for a much higher proportion of head and neck cancers with the incidence in men being almost three times that of women.

The patient when diagnosed will usually undergo a biopsy of the tumour, unless it is to be surgically removed. This tissue sample taken would be used for immunohistochemical testing with PD-L1. The testing would be done by a pathologist alongside other immunohistochemical tests which are done routinely.

The test would enable identification of those patients most likely to benefit from treatment with pembrolizumab.

**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):**

There are a number of chemotherapy regimens that are used for patients with R/M HNSCC. The National Comprehensive Cancer Network (NCCN) guidelines highlight the importance of individualised therapies based on patient characteristics, given that R/M first line patients have generally heterogeneous characteristics. The EXTREME regimen, a combination of cetuximab with cisplatin and 5-FU, is the only regimen given a Category 1 evidence-supported recommendation by NCCN. This regimen demonstrates better overall survival, objective response rate and progression free survival to other **available** regimens,

however is also associated with significantly greater frequency of grade 3/4 toxicities. Other recommendations by the NCCN guidelines include combination regimens of platinum plus taxane, cisplatin plus cetuximab and cisplatin plus 5-fluorouracil, or these agents as monotherapies. These other regimens are as toxic and some are less efficacious than the combination of cetuximab with cisplatin and 5-FU. Cetuximab is not reimbursed for this indication and provides a very limited improvement in survival with a greater increase in adverse events. Treatment decisions in advanced HNC are shaped by patient characteristics, which include their performance status (ECOG) and the goals of therapy.

**PART 6b – INFORMATION ABOUT THE INTERVENTION**

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

Pembrolizumab is a highly selective humanised monoclonal antibody that targets the PD-L1 receptor to potentiate an immune response. PD-L1 expression in HNSCC biopsies can be assessed using immunohistochemical testing with antibodies that bind specifically to the PD-L1 receptor protein.

The PD-L1 IHC 22C3 pharmDx assay was used to assess PD-L1 expression in in the KEYNOTE-048 clinical trial. Patients were enrolled into the KN048 study irrespective of PD-L1 tumour status, i.e. all comers. The PD-L1 IHC 22C3 pharmDx kit will be used to determine PD-L1 expression in order to explore the relationship between tumour PD-L1 expression and response to treatment with pembrolizumab.

Detailed information of the PD-L1 22C3 pharmDx assay kit components as well as its performance studies will be presented for MSAC consideration in the co-dependent technology submission.

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

There are currently no PD-L1 tests reimbursed by MSAC. The PD-L1 22C3 pharmDx kit is commercially available in Australia.

**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):**

Accessibility

All patients with R/M HNSCC will have a biopsy taken as part of standard practice. It is proposed that PD-L1 expression testing be carried out on the tissue sample when a patient is diagnosed with R/M HNSCC. In the KN048 study, a newly obtained biopsy is strongly preferred however an archival sample is acceptable, thus PD-L1 testing may be carried out on archival samples taken at the initial diagnosis of HNSCC.

Frequency

Only one PD-L1 test is required to identify patients who would benefit from treatment with pembrolizumab. There is no known role for PD-L1 testing in monitoring a patient's response to pembrolizumab treatment.

Further information about sample consideration

KN048 utilized PD-L1 testing on both archival and newly obtained biopsy samples. This information will be used to help inform the type of sample required for PD-L1 testing. MSD will present this information for MSAC's consideration as part of a co-dependent technology submission. In addition, the application will seek to provide information on other relevant sample considerations as needed, such as biopsy location, type of tissue and the impact of prior exposure to treatment.

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

IHC testing is a well-established technique in all major pathology labs. Laboratories already have the platform infrastructure and reagents to perform PD-L1 IHC testing. The PD-L1 antibody is the only additional resource required.

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

A certified pathologist would be responsible for conducting the testing and reporting the results.

As mentioned, IHC is a well-established technique and a common procedure. It is proposed that PD-L1 testing be eligible to be carried out in any pathology laboratory holding the appropriate accreditation to claim pathology services through the MBS.

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

It is not expected that other professionals other than certified pathologist would be able to conduct IHC testing for PD-L1 expression.

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

A certified pathologist would be responsible for conducting the test and reporting the results. Specialists involved in the diagnosis and care of patients with HNSCC including oncologists may provide a referral for PD-L1 IHC testing.

**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:**

It is expected that, consistent with the introduction of other IHC diagnostic tests for other targeted therapies, that pathologist training and quality assurance programs would be developed with respect to the delivery of diagnostic tests for PBS access to treatments targeting the PD-1 pathway in head and neck cancer. There is currently a pathologist training and quality assurance program underway for PD-L1 testing for NSCLC.

**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

It is expected that the majority of PD-L1 testing will be carried out in pathology laboratories associated with public hospitals.

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

N/A

**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):**

The comparator is no PD-L1 testing and current standard of care. As described previously, patients with R/M HNSCC receive one of many cytotoxic regimens. The choice of regimen depends on patient characteristics and clinician's choice.

- 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

Specify item number/s here

- 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):**

Patients diagnosed with R/M HNSCC are treated with one of various cytotoxic regimens, including the EXTREME regimen (cisplatin plus cetuximab plus 5-FU) or combination regimens of platinum plus taxane, cisplatin plus cetuximab and cisplatin plus 5-fluorouracil, or these agents as monotherapies. Since cetuximab is not reimbursed for this indication/line of therapy in Australia, it is seldom used. Patient factors such as age, tolerance of platinum based therapies and ECOG status play a role in determining the exact treatment provided.

- 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:**

There are currently no PD-L1 tests available in Australia. Therefore all patients with R/M HNSCC would require the PD-L1 test to be performed prior to accessing pembrolizumab.

- 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):**

There is currently no PD-L1 testing done in order to determine PD-L1 status. Patients with R/M HNSCC are currently treated with cisplatin or carboplatin together with 5-FU or a taxane, depending on patient factors and clinician choice.

Through the introduction of the proposed PD-L1 test, patients who are deemed to be PD-L1 positive will be able to access pembrolizumab monotherapy. Also, dependant on the outcomes of the KN048 study, this may also need to be applied to the combination of pembrolizumab and cisplatin and 5-FU.

**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):**

It is proposed that PD-L1 testing followed by treatment with pembrolizumab is superior to no testing and current standard of care for patients with R/M HNSCC who are PD-L1 positive. The clinical claim is justified by:

- i. Acceptable safety and analytical performance of PD-L1 test (as assessed by MSAC);
- ii. Superior efficacy with acceptable safety of pembrolizumab in PD-L1 positive patients relative to standard of care (without IHC testing) (as assessed by PBAC).
- iii. Clinical utility of the test + drug combination (To be assessed by MSAC/PBAC).

**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:** The key safety outcomes include: psychological and physical harms from testing; any adverse events related to a change in treatment including tolerability or toxicity (particularly immune related adverse events).

**Clinical Effectiveness Outcomes:** The key efficacy outcomes include: overall survival; progression free survival; quality of life; response rate (according to RECIST and immune-related RECIST criteria); duration of response.

## PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

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

It is estimated that there will be 4,955 (3,625 male) new cases of head and neck cancer in 2017 (AIHW Cancer in Australia Report, 2017). The one year survival rate for laryngeal cancer is about 85%, and for mouth cancer it is about 83%. Using these survival rates as a proxy for all R/M HNSCC, approximately 600 patients per year would be diagnosed. A more accurate estimate will be provided in the co-dependent submission.

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

As discussed previously, there is no known role for testing PD-L1 expression to monitor response to pembrolizumab treatment. As such, PD-L1 testing will be performed once only to determine patient eligibility to receive treatment with pembrolizumab.

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

It is proposed that the PD-L1 test will be required once only per patient.

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

As per Q 47 above, approximately 600 patients would utilise the PD-L1 test in the first year.

### **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:**

The clinical claim is that PD-L1 testing and treatment with pembrolizumab is superior to current standard of care. Thus, pembrolizumab could replace current standard of care in PD-L1 positive R/M HNSCC patients. It is estimated that the uptake of PD-L1 testing would be 100% for all patients diagnosed with R/M HNSCC. The risk of leakage for PD-L1 testing is negligible as testing would be restricted to those patients who are potentially eligible for pembrolizumab as requested.



## PART 8 – COST INFORMATION

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

The expected fee for the proposed service is consistent with other immunohistochemical tests reimbursed by the MBS.

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

The IHC test for PD-L1 expression can take between 2.5-4 hours depending on instrumentation and protocol used.

**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: Immunohistochemical examination of biopsy material by immunoperoxidase or other labelled antibody techniques using the PD-L1 antibody to determine if the requirements relating to programmed cell death ligand 1 (PD-L1) status for access pembrolizumab under the Pharmaceutical Benefits Scheme (PBS) are fulfilled.

Fee: \$ (to be determined)

## PART 9 – FEEDBACK

The Department is interested in your feedback.

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

Approximately 2 weeks to obtain the necessary information and to write up.

**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