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Public Summary Document

Application No. 1527 – somatic gene testing of central nervous system tumours and sarcomas

**Applicant: The Royal College of Pathologists of Australasia (RCPA)**

**Date of MSAC consideration: MSAC 76th Meeting, 1-2 August 2019**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](http://www.msac.gov.au/)

# Purpose of application

An application for a specified number of genetic tests for the diagnosis and prognosis of central nervous system neoplasms, and for specified number of genetic tests prognostic testing in patients with sarcomas, was received from the Royal College of Pathologists in Australasia (RCPA) by the Department of Health.

The proposed medical services would provide genetic testing for:

* identification of 1p/19q co-deletion status in patients with suspected oligodendroglioma
* identification of *IDH1* and *IDH2* mutation in patients with glioma or glioblastoma
* identification of *MGMT* promoter methylation status in patients with glioblastoma
* identification of the gene copy number of *MDM2*, and gene rearrangements of *FUS*, *DDIT3*, *EWSR1*, *ETV6*, *NTRK1, NTRK3*, SS18, *STAT6, PAX3, PAX7, BCOR, CIC, HEY1, ALK, USP6, NR4A3, NCOA2,* *COL1A1* and *PDGFB* in patients with sarcomas.

This application was considered in conjunction with Applications 1526 and 1528.

# MSAC’s advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness and cost-effectiveness, MSAC supported 17 of the 19 requested MBS items proposed by the MSAC Executive overall. Two requested MBS items were deferred, relating to hydatidform mole (application 1528) and analogue secretory carcinoma (application 1528), in order to seek more information in order to clarify the appropriate test usage and item descriptor wording.

| **Consumer summary** |
| --- |
| Cancer arises when cells develop genetic changes that cause abnormal growth. A somatic cell is any cell in the body that is not an egg or sperm cell, and gene mutations which develop in - cells after the egg is fertilised are called “somatic mutations”. Somatic tumour testing is where a piece of a tumour is tested to look at the somatic mutations in the cancer cells. These tests can help provide patients with an appropriate diagnosis. Applications 1526, 1527 and 1528 are for somatic tumour testing for rare cancers. They have been grouped together because the numbers of patients with these cancers is too small to consider each application on its own.**MSAC’s recommendation to the Commonwealth Health Minister**MSAC recommended some changes to the wording in the MBS descriptors, to ensure consistency and appropriate setting of fees when testing for these somatic gene mutations. |

MSAC supported the following listings for Application 1527.

| Category 6 – (Group P7 Genetics) – Pathology services |
| --- |
| XXXXX-08Analysis of tumour tissue from a patient with clinical or laboratory evidence, including morphological features, of glial neoplasm with probable oligodendroglial component, as requested by a specialist or consultant physician, for the detection of chromosome 1p/19q co-deletion.Maximum one test per lifetimeFee: $340 |
| XXXXX-09Analysis of tumour tissue from a patient with clinical or laboratory evidence, including morphological features, of glial neoplasm, as requested by a specialist or consultant physician, for the identification of *IDH1/2* pathological variant status if IDH1 (R132H) immunohistochemistry is negative.Maximum one test per lifetimeFee: $340 |
| XXXXX-10Analysis of tumour tissue from a patient with clinical or laboratory evidence, including morphological features, of glioblastoma, as requested by a specialist or consultant physician, for the characterisation of *MGMT* promoter methylation status.Maximum one test per lifetimeFee: $400 |
| XXXXX-11Analysis of tumour tissue from a patient with clinical or laboratory evidence, including morphological features, of sarcoma, as requested by a specialist or consultant physician, for the characterisation of one or more of the following molecular changes; copy number changes or gene rearrangements; or other molecular changes:1. *MDM2* CNV;
2. *FUS*;
3. *DDIT3*;
4. *EWSR1*;
5. *ETV6*;
6. *NTRK1*
7. *NTRK3*;
8. *COL1A1*;
9. *PDGFB*;
10. *STAT6*;
11. *PAX3*;
12. *PAX7*;
13. *SS18*;
14. *BCOR*;
15. *CIC*;
16. *HEY1*;
17. *ALK*;
18. *USP6*;
19. *NR4A3*;
20. *NCOA2.*

Maximum one test per lifetimeFee: 1 gene - $340; 2 to 3 genes - $400; 4 or more genes - $800 |

# Summary of consideration and rationale for MSAC’s advice

MSAC noted that the proposals for 19 new MBS items from the MSAC Executive spanned three applications:

Application No. 1526 – Somatic gene testing of haematological malignancies

Application No. 1527 – Somatic gene testing of central nervous system tumours and sarcomas

Application No. 1528 – Somatic gene testing of hydatidiform mole, granulosa cell tumour of the ovary, midline squamous cell carcinoma, salivary gland carcinoma, secretory carcinoma of the breast and renal cell carcinoma.

MSAC noted that there has been a long history of meetings for these applications. The requested MBS items are for rare tumours with low mutation frequencies, so they have been pragmatically grouped together.

MSAC affirmed the importance of ensuring that appropriate quality assurance programs are established for all gene testing as part of the implementation of the proposed MBS items.

MSAC noted that its task is to check that each item descriptor is appropriate. The RCPA has had its feedback already incorporated into the proposed descriptors.

MSAC advised the following as being applicable across all relevant MBS items:

for testing for a rearrangement in a single gene, the fee should be $340 (reflecting a slightly higher fee than the MBS item number for ISH for HER2 and in doing so establishing a benchmark); for a panel testing 2–3 genes, the fee should be $400 (reflecting the lowest requested fee for testing 3 gene); and for a panel testing 4 or more genes, the fee should be $800 (reflecting the lowest requested fee for testing 4 or more genes)

if a descriptor is referring to a single gene, then write the gene into the text (not in a bulleted list)

if it is referring to more than one gene, then write the genes in a list without the word “or” between each gene

change “characterisation of one or more of the following gene rearrangements” to “characterisation of gene rearrangements in one or more of the following” and remove the word “or” between each gene in the list that follows

change “mutation” to “pathogenic variant”

state that there is a maximum of one test per lifetime.

In addition to the above changes, the following specific amendments were proposed:

XXXXX-01 – “laboratory evidence” should be defined as being “not negative on immunohistochemistry”

XXXXX-01 – this item cannot be co-claimed with XXXXX-02, so a note to this effect should be added

XXXXX-02 – this item cannot be co-claimed with XXXXX-01, so a note to this effect should be added

XXXXX-04 – change “the characterisation of i(q7) gene rearrangement” to “the presence of isochromosome 7q”

XXXXX-08 – keep “glioma or glioneural tumours” (not “oligodendroglioma”) and use “detection” instead of “characterisation”

XXXXX-13 – the fee should be benchmarked to the fee of $250 (reflecting MBS items 73348 and 73350, which both specify the detection of known gene variants in diagnosing cystic fibrosis), and “characterisation” should be replaced with “detection”.

MSAC noted the Department’s concerns that the proposed descriptor for XXXXX-11 does not limit the number of genes that may be tested. While this permits the testing of a greater number of clinically relevant genes, this descriptor may lead to a risk of leakage for testing of gene mutations where there is no evidence of clinical utility. However, MSAC noted that a panel test will be required in most cases, and the costing of testing extra genes should not result in an increase beyond the recommended fee of $800.

MSAC considered that XXXXX-17 appears to be a duplicate of XXXXX-15 for analogue secretory carcinoma, so needs to be removed or amended to clarify the intended difference.

MSAC considered that XXXXX-12 for hydatidiform mole should be re-visited because it did not adequately address either the likelihood of recurring disease needing repeat testing (and thus the increased possibility of false negative clinical conclusions) or the need for samples from the parental source.

MSAC advised that, as a general principle, these tests are for once in a lifetime. It was noted that some might patients may need another test if metastasis is present; however, MSAC did not support these items being used for monitoring. It is possible that, on relapse, retesting may be desirable. MSAC advised that this should not be accommodated now because MSAC could not support the consequential delay in implementing these applications for initial diagnosis.

# Background

An application for MBS funding of the requested genetic tests has not previously been made to the Medical Services Advisory Committee (MSAC).

Applications 1526, 1527 and 1528 were created from an earlier, larger application 1459 (now retired), submitted by the RCPA in November 2017. Application 1527 seeks public funding for somatic testing of tumour tissue grouped as CNS tumours and sarcomas.

A PICO Confirmation was created for each of the three applications, and discussed at the PASC meeting of 12 April 2018. The PASC discussion highlighted that, at that time, the three applications did not adequately address the clinical utility of each requested genetic test.

Following this PASC outcome, and consideration by the MSAC Executive in June 2018, the Department and the Applicant, together with other stakeholders, convened a workshop on 16 May 2019, the “Pathology Pilot Meeting”. Amongst other things, this workshop considered each application, to determine the clinical utility of each of the separate tests, and their place in current clinical practice. To facilitate this discussion, and explore how best to identify the type and nature of the clinical utility of future requests for MBS funding of genetic tests, the workshop was guided by an approach developed by Medex Consulting (provided to the MSAC Executive at its meeting of 3 May 2019). Ahead of the workshop, a triage table of expected clinical utility type(s) was drafted encompassing each requested test. Based on feedback before and after the workshop, this table was updated for each of the requested tests and incorporates the advice of Medex Consulting, the applicant, other stakeholders, and the Department.

At the workshop, the Department proposed that the application would be considered for expedition through the MSAC process if the MSAC Executive was also agreeable with this approach.

## Current funding arrangements

The genetic tests proposed in the application are currently provided by the States and Territories, often being conducted through public hospital genetic services, or otherwise through private pathology providers.

# Prerequisites to implementation of any funding advice

Neither the PICO nor the MSAC Executive discussion addressed the regulatory and/or accreditation requirements associated with the provision of any of the proposed tests.

# Proposal for public funding

The PASC process was used for this application, but given the status of testing in the Australian context, the nature of the genetic tests proposed, and following discussions both at the Pathology Pilot Meeting and by the MSAC Executive, a full HTA assessment was not undertaken.

The requested MBS item descriptors are presented in Table 1. The item descriptors suggested by the Department are presented in Table 2.

**Table 1: Requested MBS item descriptors, per the application form**

| Category 6 –Genetics P7 |
| --- |
| Detection of chromosome co-deletion 1p/19q in the initial assessment of patients with laboratory evidence of CNS gliomas and glioneuronal tumours,**AND/OR**Identification of IDH1/2 mutation status, if IDH (R132H) immunohistochemistry (IHC) is negative, in the initial assessment of patients with laboratory evidence of a CNS glioma,**AND/OR**MGMT promoter methylation status in the assessment of patients with laboratory evidence of glioblastoma.Fee: $454 (for each) |
| In the initial assessment of patients with laboratory evidence of soft tissue and bone tumours, identification of gene rearrangement or copy number changes of:MDM2, FUS, DD1T3, EWSR1, ETV6, NTRK3, COLIA1 and PDGF.Fee: $1,200 *(if listed as a panel)* |
| In the assessment of patients with laboratory evidence of soft tissue and bone tumours, identification of gene rearrangement or copy number changes of:* MDM2

**AND/OR*** FUS

**AND/OR*** DD1T3

**AND/OR*** EWSR1

**AND/OR*** ETV6

**AND/OR*** NTRK2

**AND/OR*** COLIA1

**AND/OR*** PDGF

$454 *(if listed as separate items)* |

Subsequent to the MSAC Executive meeting, the RCPA provided feedback to the Department and confirmed the expansion of the gene tests for the diagnosis of sarcomas to include the tests in table 2 below.

**Table 2: Department-suggested MBS item descriptors**

| Category 6 –Genetics P7 |
| --- |
| XXXXX-08Analysis of tumour tissue from a patient with clinical or laboratory evidence of glioma or glioneural tumours, as requested by a specialist or consultant physician, for the characterisation of chromosome co-deletion 1p/19q.Maximum one test per lifetimeFee: $xxx.xx Benefit: 75% = $xxx.xx 85% = $xxx.xx. |
| XXXXX-09Analysis of tumour tissue from a patient with clinical or laboratory evidence of glioma, as requested by a specialist or consultant physician, for the characterisation of IDH1/2 mutation status if IDH1 (R132H) immunohistochemistry is negative.Maximum one test per lifetimeFee: $xxx.xx Benefit: 75% = $xxx.xx 85% = $xxx.xx. |
| XXXXX-10Analysis of tumour tissue from a patient with clinical or laboratory evidence of glioblastoma, as requested by a specialist or consultant physician, for the characterisation of MGMT promoter methylation status.Frequency of testing?Fee: $xxx.xx Benefit: 75% = $xxx.xx 85% = $xxx.xx. |
| XXXXX-11Analysis of tumour tissue from a patient with clinical or laboratory evidence of sarcoma, as requested by a specialist or consultant physician, for the characterisation of one or more of the following molecular changes; copy number changes or gene rearrangements including but not limited to:1. *MDM2* CNV; or
2. *FUS*; or
3. *DDIT3*; or
4. *EWSR1*; or
5. *ETV6*; or
6. *NTRK1*; or
7. *NTRK3*; or
8. *COL1A1*; or
9. *PDGFB*; or
10. *STAT6*; or
11. *PAX3*; or
12. *PAX7*; or
13. *SS18*; or
14. *BCOR*; or
15. *CIC*; or
16. *HEY1*; or
17. *ALK*; or
18. *USP6*; or
19. *NR4A3*; or
20. *NCOA2*

Maximum one test per lifetimeFee: $xxx.xx Benefit: 75% = $xxx.xx 85% = $xxx.xx. |

# Summary of public consultation feedback/consumer issues

There was no external consultation sought for this application beyond the stakeholders attending the “Pathology Pilot Meeting” held at the RCPA on 16 May 2019.

# Proposed intervention’s place in clinical management

The most recent version of the World Health Organization classification of tumours of the central nervous system defines the morphological subtypes of this group of cancers and their genetically distinct variants. By virtue of their place in the WHO Guidelines, the proposed genetic tests have documented known significance in each of the diseases specified; there are no tests proposed in the application with variations of unknown significance. The same conclusion can be drawn on a similar basis for the proposed genetic tests for sarcoma.

The clinical utility of each test, and the place of each test in a diagnostic algorithm in contemporary Australian practice, were discussed and confirmed by the pathology and specialist physicians at the Pathology Pilot Meeting and with reference to published literature.

# Comparator

The comparator for this application is “no genetic testing” for each of the genetic abnormalities described.

# Comparative safety

For this application, there was no assessment of the comparative safety of testing. The application stated that, for each investigation “(t)he proposed test involves equivalent safety issues to current tissue pathology investigations”.

## Test adverse events

Each of the proposed tests is to be performed on a tissue specimen, the exact nature depending on the disease type, which would already have been taken for the purposes of tumour morphological assessment. It is not expected that there would be adverse events directly associated with testing. However, if a sample is insufficient or of too poor quality, a second sample may be required to provide results.

The main downstream effect of the proposed test is to provide a definitive diagnosis for the patient and thus inform subsequent patient interactions and management. Where the test results in a diagnosis associated with a poor prognosis, the test result is expected to be delivered by a specialist physician who can counsel the patient appropriately.

## Adverse events from change in management

Among the proposed tests, predictive value for a change in patient treatment is anticipated for with use of the 1p/19q deletion test, *IDH1*/*IDH2* mutation, *MGMT* methylation status and *PDGFB*.

There are no adverse consequences anticipated from the use of any of the proposed tests. None of the proposed tests are considered experimental, nor is their use anticipated to directly lead to access to therapies which are not currently approved for use in Australia.

# Comparative effectiveness

## Direct effectiveness

According to the supportive guidance documents and published literature, each of the tests with the exception of *MGMT* methylation status which is not included in the current WHO guideline, is use for diagnostic purposes. In addition, each of the CNS tumour tests, including *MGMT* methylation, has both prognostic and predictive value[[1]](#footnote-1).

The WHO sarcoma guideline also subtypes these tumours according to tests which are considered to have satisfactory diagnostic and prognostic and/or predictive value.

**Clinical claim**

The application stated that the overall clinical claim was for superiority over not testing for each of the genetic defects described.

# Economic evaluation

The MSAC Executive advised that, in the context of clear clinical utility and low costs of testing overall, a full economic evaluation was not warranted for this application.

# Financial/budgetary impacts

An epidemiological approach has been used to estimate the financial implications of listing each of the proposed tests on the MBS.

The Australian Institute of Health and Welfare (AIHW) cancer data summary was used to estimate the incidence of patients with each tumour type, shown in Tables 3 and 4 below[[2]](#footnote-2).

Based on complete data for 2014 (subsequent years are incomplete), the AIHW estimated the incidence of soft tissue sarcoma at 1527 cases. As per the tests included in the request item(s) for sarcoma, the subtypes of sarcoma in which the proposed tests are to be used are shown in Table 3[[3]](#footnote-3):

**Table 3: Estimated proportion of sarcoma subtypes**

| **Sarcoma subtype** | **Gene defect(s)** | **Proportion of all sarcomas** |
| --- | --- | --- |
| Atypical lipomatous tumour/ dedifferentiated liposarcoma | *MDM2* CNV | 15%[[4]](#footnote-4) |
| Myxoid/round cell liposarcoma  | *FUS*, *DDIT3*, *EWSR1* |
| Infantile fibrosarcoma | *ETV6*, *NTRK1, NTRK3* | 0.2%[[5]](#footnote-5) |
| Dermatofibrosarcoma protuberans | *COL1A1*, *PDGFB* | 5%7 |
| Ewing sarcoma | *ALK, EWSR1, HEY1, PAX3, PAX7, BCOR, USP6* | 4%7 |
| Myxoid sarcoma | *NR4A3* | 2%8 |
| Sinonasal sarcoma | *PAX3* | <1%8 |
| Rhabdomyosarcoma | *PAX7* | 3%8 |
| Synovial sarcoma | *SS18* | 2%8 |
| Solitary fibrous tumour | *STAT6* | 1%8 |
| Ewing-like sarcoma | *CIC* | <1%8 |
| Uterine  | *NCOA2* | 3%8 |
| Renal sarcoma | *NCOA2* | 5%8 |

Based on complete data for 2015 (subsequent years are incomplete) the AIHW estimated the incidence of all ‘brain cancers’ (CNS tumours) to be 1787 cases. The following proportions were obtained from the literature.

* The proportion of all CNS tumours that are gliomas is 40%.[[6]](#footnote-6)
* The proportion of all CNS tumours that are glioblastomas is 15%.6
* The proportion of gliomas that are IDH wild type is 18% (i.e. those that would be expected to be IDH1 (R132H) IHC negative and require the proposed test).[[7]](#footnote-7)
* The proportion of glioblastomas that are IDH wildtype is 90% (i.e. those that would be expected to be IDH1 (R132H) IHC negative and require the proposed test).6

**Table 4: Estimated disease incidence and number of tests to be performed annually**

| **Genetic test(s)** | **Tumour type** | **Estimated number of new cases per year (n)** | **Estimated number of tests per year (n)** |
| --- | --- | --- | --- |
| 1p/19q | Oligodendroma  | 715 | 715 |
| *IDH1/ IDH2* | Glioma & glioblastoma | 715 (glioma)268 (glioblastoma)Total = 983 | 129 (glioma)241 (glioblastoma)Total = 370 |
| *MGMT* | Glioblastoma | 268 | 536(assuming all patients relapse in the first year and all require re-testing) |
| *MDM2* CNV, *FUS, DDIT3, EWSR1, ETV6, NTRK1, NTRK3, SS18, STAT6, PAX3, PAX7, BCOR, CIC, HEY1, ALK, USP6, NR4A3, NCOA2, COL1A, PDGFB* | Sarcoma subtypes | 613 | 613 |

# MSAC Executive discussion

| **MSAC Executive key issue** | **MSAC Executive advice to MSAC** |
| --- | --- |
| Clinical claim reasonable | The current WHO Classification of Tumours of the Central Nervous System and Classification of Tumours of Soft Tissue and Bone provide the appropriate standards of clinical care for Australian patients for these conditions.The use of *MGMT* methylation status to direct treatment choices in patients with glioblastoma is incorporated into current Australian clinical practice guidelines. |
| Testing methodology | The MBS item descriptors in the application reasonably did not include a testing method for any of the tests. |
| Determination of clinical utility and diagnostic performance | The Department and applicant had agreed an approach to the determination of clinical utilities for each of the proposed tests, based on a triage assessment developed prior to, and discussed at, the Pathology Pilot Meeting. The entry of each test in the WHO Guidelines was accepted to provide sufficient demonstration of its diagnostic performance, and also its clinical validity and/or clinical utility. Further assessment of these aspects was therefore not sought for this application. |
| Limitations on number of tests | Each of the tests described are proposed to be performed once per patient lifetime, with the exception of *MGMT* promoter methylation status which is assessed at initial diagnosis and upon relapse. |
| Funding of genetic tests for sarcoma | The appropriate method of funding the sarcoma gene tests either individually or as a panel remains under discussion between the applicant and the Department. |
| Economic evaluation and financial analysis | Given the relatively small patient populations of each disease type who require each genetic test, the estimated fee for each service involving an individual test, and the estimated total annual cost of funding all the tests in the application, it was proposed by MSAC Executive that a full HTA assessment would not be required prior to consideration of funding by MSAC. |
| Uncertainty with financial inputs | Given the estimated very low incidence of the sarcoma tumour types described, and a lack of registry data, there may be variability in the number of patients who require testing. However, based on available data, the number of tests per year is not expected to be substantially larger than described for sarcoma and the identified CNS tumours. |

At its 21 June 2019 teleconference, the MSAC Executive noted that the purpose of the application is to seek Medicare Benefits Schedule (MBS) listing of genetic testing of certain central nervous system (CNS) tumours and in sarcomas.

The MSAC Executive noted the most recent classification of CNS tumours by the World Health Organization (WHO)[[8]](#footnote-8) which serves as the recognised diagnostic algorithm used in Australia and the description of MGMT promoter methylation status by Hegi[[9]](#footnote-9). The MSAC Executive also noted the most recent WHO classification of sarcoma[[10]](#footnote-10). The MSAC Executive accepted that these WHO Guidelines only include genetic biomarkers into their classification when these biomarkers have been shown to have prognostic and/or predictive value.

The MSAC Executive noted that:

* The WHO Guideline for CNS tumours describes the diagnostic algorithm for glioma and glioblastoma according to 1p/19q and *IDH1*/*IDH2* status.
* The WHO Guideline for CNS tumours recommends *IDH1*/*IDH2* status to be determined in patients with a negative IDH1 (R132H) immunohistochemistry test.
* *MGMT* promoter methylation status is incorporated into Australian guidelines for the management of patients with glioblastoma as being predictive for the likelihood of response to temozolomide[[11]](#footnote-11).
* That *MDM2*, *FUS*, *DDIT3*, *EWSR1*, *ETV6*, *NTRK3*, *COL1A1* and *PDGFB* molecular changes, either individually or in combination, are diagnostic tests used for the classification of a number of sarcomas.

The MSAC Executive noted that, when used as proposed, each of the tests above would be performed once in an individual patient’s lifetime. The exception is *MGMT* status, which could be assessed twice: at the initial diagnosis of glioblastoma and at disease relapse.

The MSAC Executive agreed with the Department’s determination of the clinical utility for each of the proposed tests as having been comparatively assessed in published literature, demonstrated by their inclusion in the relevant WHO Guidelines documents.

The MSAC Executive therefore advised that each of the proposed tests offers superior effectiveness and non-inferior safety compared with no testing.

The MSAC Executive also advised that the financial impact analysis was sufficiently accurate to be relied upon to inform decision-making.

The Executive noted that the Australian diagnostic definitions of CNS tumours in this application are based on the current WHO guideline. Similarly, the use of MGMT methylation status for prognostic testing of patients with glioblastoma in current Australian clinical practice is established in current clinical practice.

Given that the WHO guidelines subtypes the CNS tumours and sarcomas according to tests which are considered to have satisfactory diagnostic, and/or prognostic and/or predictive performance, the Executive advised that the proposed tests in this application should not be re-examined in this regard.

Given the estimated fee per test, the likely single use of most of the tests per patient lifetime, and the relatively small size of the populations anticipated requiring each test, the MSAC Executive advised that further assessment of the application, including by the Evaluation Sub-Committee would not be necessary and that it could proceed directly to the full MSAC for consideration.

The MSAC Executive deferred any consideration as to the appropriate method of funding the sarcoma gene tests as either individual tests or as a panel, pending further negotiation between the applicant and the Department on their consequences for the fees and thus the cost per patient.

A further discussion on the three applications to finalise the item descriptor wording was held at the MSAC Executive meeting on 16 August 2019.

# Other significant factors

Nil.

# Applicant’s comments on MSAC’s Public Summary Document

The College would like to take this opportunity to thank the Department and the MSAC for their assistance in moving this application forward to a successful outcome that will deliver great benefits for a small group of vulnerable patients. The College is seeking clarification on a number of issues, which may be crucial in the drafting of the item number descriptors.

# Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website:
[visit the MSAC website](http://www.msac.gov.au/)

1. https://oncologypro.esmo.org/Education-Library/Factsheets-on-Biomarkers/MGMT-Promoter-Methylation-in-Glioma [↑](#footnote-ref-1)
2. https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/contents/summary [↑](#footnote-ref-2)
3. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology Soft Tissue Sarcoma. Version 2.2019 –February 4, 2019. https://www.nccn.org/professionals/physician\_gls/pdf/sarcoma.pdf [↑](#footnote-ref-3)
4. Ducimetiere, F. et al. Incidence of Sarcoma Histotypes and Molecular Subtypes in a Prospective Epidemiological Study with Central Pathology Review and Molecular Testing. PLoS One 2011; 6(8): e20294 doi: 10.1371/journal.pone.0020294 [↑](#footnote-ref-4)
5. Loeb, D. Thornton, K. & Shokek, O. Pediatric Soft Tissue Sarcomas. Surg Clin North Am. 2008 Jun; 88(3): 615–vii. doi: 10.1016/j.suc.2008.03.008 [↑](#footnote-ref-5)
6. The 2016 World Health Organization Classification of Tumours of the Central Nervous System: a summary. Acta Neuropathology Feb 2016 DOI 10.1007/s00401-016-1545-1 [↑](#footnote-ref-6)
7. Paul, Y. et al. DNA methylation signatures for 2016 WHO classification subtypes of diffuse gliomas. Clinical Epigenetics 2017; 9: 32 [↑](#footnote-ref-7)
8. The 2016 World Health Organization Classification of Tumours of the Central Nervous System: a summary. Acta Neuropathology Feb 2016 DOI 10.1007/s00401-016-1545-1 [↑](#footnote-ref-8)
9. Hegi. MGMT Gene Silencing and Benefit from Temozolomide in Glioblastoma. NEJM 2005;352:997-1003 [↑](#footnote-ref-9)
10. WHO Classification of Tumours of Soft Tissue and Bone. Fourth Edition. 2013. ISBN-1 9789283224341 [↑](#footnote-ref-10)
11. https://www.eviq.org.au/medical-oncology/neurological/glioma/3364-glioblastoma-temozolomide-chemoradiation-foll [↑](#footnote-ref-11)