



Australian Government

Medical Services Advisory Committee

## **MSAC Public Summary Document**

### ***Application No. 1267 – HbA1C testing for the diagnosis of diabetes mellitus***

**Sponsor/Applicant/s:** Australian Diabetes Society, the Royal College of Pathologists of Australasia and the Australasian Association of Clinical Biochemists

**Date of MSAC consideration:** MSAC 61st Meeting, 3-4 April 2014

#### **1. Purpose of application**

An application requesting MBS listing of HbA1c testing for the diagnosis of diabetes mellitus (diabetes) was received from the Australian Diabetes Society, the Royal College of Pathologists of Australasia and the Australasian Association of Clinical Biochemists by the Department of Health in May 2012.

The Department and the applicant agreed that assessment of HbA1c point-of-care testing (PoCT) was out of scope for this application.

#### **2. Background**

MSAC has not previously considered HbA1c testing for the diagnosis of diabetes mellitus.

HbA1c testing for management of diabetes is MBS listed under Category 6: Pathology Services, item 66551.

#### **3. Prerequisites to implementation of any funding advice**

An assay designed for HbA1c testing is classified as a Class 2 in vitro diagnostic medical device (IVD). The Therapeutic Goods Administration (TGA) regulatory framework for IVDs changed in July 2010. As the test was available before July 1 2010, it is currently exempt from registration on the register of therapeutic goods in Australia, however, will be required to be registered by June 2014.

The test would be performed in NATA accredited laboratories, consistent with MBS item 66551, or alternatively performed at the point-of-care, as MBS item 73840 which is funded under the Quality Assurance for the Aboriginal and Torres Strait Islander Medical Services (QAAMS).

#### 4. Proposal for public funding

The application's proposed listing was for two new MBS items for quantitation and confirmation of HbA1c (glycated haemoglobin) performed for the diagnosis of diabetes.

The proposed MBS items were for:

- initial testing, which would be limited to one test per year for an asymptomatic patient, with repeat testing allowed if the patient is symptomatic and the first test result is negative; and
- confirmatory testing, which would be limited to patients in which the initial test is positive.

The Department advised that due to these proposed limitations, it would not be possible to amend the existing HbA1c testing item for management of diabetes, as this has different limitations (four times per year, per patient).

The proposed fee was \$16.80, the same as the existing HbA1c MBS item.

The application also proposed that in the existing MBS item for HbA1c, the term 'glycosylated' is replaced with 'glycated', better reflecting current terminology.

##### **Application proposed MBS item descriptors for HbA1c testing for diagnosis of diabetes**

Category 6 – Pathology Services Group P2- Chemical	
MBS xxxxx	
Quantitation of HbA1c (glycated haemoglobin) performed for the diagnosis of diabetes in patients at high risk, as determined by the AUSDRISK screening tool or according to NHMRC guidelines	
Fee: \$16.80	
Limit: one per person, per year if the patient is asymptomatic, but would allow a repeat test if the patient is symptomatic and the first test result is negative.	
Category 6 – Pathology Services Group P2- Chemical	
MBS xxxxx	
Confirmation of HbA1c (glycated haemoglobin) quantitation performed for the diagnosis of diabetes in patients at high risk, as determined by the AUSDRISK screening tool or according to NHMRC guidelines	
Fee: \$16.80	
Limit: one per person, per year upon an initial positive test	

PASC noted that it was important to limit the frequency of testing, because there was potential for a perverse incentive to more frequently order the HbA1c test, in case this identifies more patients to be eligible for the current diabetes service incentive payments (SIP) for the management of established diabetes.

#### 5. Summary of Consumer/Consultant Feedback

Consultation feedback on the proposal was very positive and no significant foreseeable disadvantages were noted.

It was noted that the proposal will improve and simplify the diagnosis of diabetes mellitus. There was strong agreement with the clinical claim - that HbA1c test is more efficient and convenient than current diagnostic tests, as it involves the use of a random blood sample

which can be taken from a patient at any time without further preparation. Public consultation noted that this would improve the patient's experience as well as lead to more consistent diagnosis of T2DM.

There was some concern that the application seeks to confine testing to laboratory based measurements and specifically seeks to prevent reimbursement for clinic or surgery based HbA1c measurement. Public consultation noted that this restriction would cause substantial disadvantage to patients who are based in rural and remote locations.

## **6. Proposed intervention's place in clinical management**

The application proposed that the intervention would form part of case detection in diabetes. Currently case detection, according to NHMRC guidelines, is performed through a three stage process of risk assessment and two blood tests (one plasma glucose test followed by confirmatory tests, either: another plasma glucose test on a separate occasion; or, a glucose tolerance test). In some patients, a third test may be required (if the initial plasma glucose test suggests diabetes, and the follow-up plasma glucose test is equivocal, then the patient should have an OGTT).

The addition of HbA1c testing in patients with confirmed diabetes to assess severity is not part of the NHMRC case detection Guidelines, however, it is recommended in the NHMRC blood glucose control guidelines that HbA1c measurements be used to assess long term blood glucose control. It is therefore reasonable that an initial HbA1c test would be performed in those patients diagnosed by the current case detection methods, which would not be required if the patient has undergone the HbA1c test as part of diagnosis.

The application claimed that fewer return visits to the practitioner would be required if HbA1c is used as the diagnostic test, as it diagnoses and assesses severity in the one test, enabling the practitioner to enact management on the confirmatory test return visit. This application claimed this could result in cost savings for the MBS by reducing the number of consultations.

The diagnostic pathway will rely on the guidance given by the Australian Diabetes Society (or new NHMRC Guidelines) should the HbA1c test become available for the diagnosis of diabetes.

The application suggested that a third test should be conducted if a patient has one HbA1c test in the diagnostic range and the confirmatory test in the no diabetes range (this will have cost ramifications). This would also apply to the current diagnostic regimen and this is covered in the Guidelines (Colagiuri et al 2009a).

## **7. Comparator**

The application's nominated comparator for the intervention was two blood glucose measures: the fasting plasma glucose (FPG) test and the oral glucose tolerance test (OGTT). Both tests are done routinely in Australia, are listed on the MBS (FPG item number 66500 and OGTT item number 66542) and are recommended for use by Australian guidelines. The HbA1c test is intended as an alternative to these tests in the diagnostic pathway for the majority of the population.

MSAC considered that these were appropriate comparators, however noted that FPG and OGTT are flawed reference standards because of the higher coefficient of variability (CV) compared to HbA1c testing which reflects greater inconsistency in reproducing results. MSAC agreed that diagnosis of a diabetic complication such as retinopathy was a more objective reference standard against which to compare HbA1c testing for assessment of the clinical effectiveness, safety and cost effectiveness.

## 8. Comparative safety

No studies were identified that could inform an assessment of the safety of HbA1c testing compared to FPG and/or OGTT testing in the diagnosis of diabetes. There is some risk associated with venepuncture, however this is the same for all three tests. There are also risks associated with OGTT such as gastro-intestinal discomfort and additional blood collections which are unique to that test.

MSAC noted that the HbA1c test is available and widely used in Australia for monitoring of diabetes, and that it has the same or less risk than the comparators, therefore safety was not considered a major concern.

## 9. Comparative effectiveness

Three studies (McCance et al. 1994, Engelgau et al. 1997, Massin et al. 2011) were identified to inform the comparison of diagnostic accuracy between HbA1c testing and the comparators, with retinopathy as the reference standard. The body of evidence was of poor quality, the studies were dated and there was considerable variability between studies in the accuracy results. However, the studies were consistent in that there was no difference in the discriminatory power of the tests used for predicting retinopathy.

### Results from three studies comparing diagnostic accuracy of blood glucose measures against reference standard of retinopathy

Study	ROC cutoff points	Sensitivity	Specificity	Other data
McCance et al. 1994	Optimal: FPG:7.2mmol/l 2hPG:13.0mmol/l HbA1c:7.0%	81.3% 87.5% 78.1%	81.4% 80.4% 84.7%	
	WHO diagnostic: FPG:6.8mmol/l 2hPG:11.1mmol/l HbA1c:6.1%	81.2% 87.5% 81.3%	77.1% 75.8% 76.8%	
Engelgau et al. 1997	FPG:125mg/dL 2hPG:200mg/dL HbA1c:6.5%	57% 51% 51%	88% 89% 86%	
DESIR Massin et al. 2011	FPG: 108mg/dL HbA1c: 6.0%	27% 19%	88% 92%	PPV 8.4%, NPV 97% PPV 6.0%, NPV 92%
	FPG: 116mg/dL HbA1c: 6.5%	19% 9%	97% 98%	PPV 14.0%, NPV 96% PPV 14.8%, NPV 97%
	Area under ROC: FPG: 0.64 HbA1c: 0.64			

PPV- positive predictive value; NPV- negative predictive value; ROC- receiver operating characteristic 2hPG - 2h plasma glucose

A further paper, which was not included in this application but supported the above results, provided a pooled analysis from nine studies around the world (DETECT-2) and was the basis for Australian recommendations to use HbA1c for diagnosis (d'Emden et al. 2012). It was also included in the systematic review that informed the World Health Organization's recommendations for using HbA1c for diagnosis. The analysis found that the overall discriminatory power for predicting retinopathy (measured by the area under the curve in a ROC analysis) for each of the glucose measures was uniformly high (HbA1c: 0.90, 95% CI: [0.88,0.92]; FPG: 0.87, 95%CI: [0.85,0.89]; 2hPG: 0.89, 95% CI: [0.87, 0.91]) and not statistically significantly different from one another.

The diagnostic accuracy was compared in studies that did not have a retinopathy reference standard. Although the evidence was poor, it was consistent in showing that HbA1c is equivalent to FPG and OGTT. Where a reference standard wasn't used, the results were very heterogeneous, concordance between the tests was poor and it was difficult to draw any conclusions.

MSAC noted that there is little difference between the discriminatory power of FPG, 2hPG and HbA1c to predict retinopathy, despite there being considerable discordance when the tests are compared to one another for diagnosis. Three major international organisations have already recommended HbA1c for diagnosis on the basis of the strength of the relationship between it and retinopathy.

MSAC accepted that although the evidence presented demonstrated that the ability of all blood glucose measures to predict retinopathy was relatively poor, the performance of HbA1c testing was equivalent to FPG and OGTT.

## **10. Economic evaluation**

The application presented a cost-utility analysis to assess the comparative costs and benefits associated with HbA1c testing in the diagnosis of diabetes, compared to FPG and OGT testing, in the Australian health care setting. The modelled benefits from testing for diabetes included:

1. The diagnosis of diabetes prior to symptom development, so as to enable control of blood glucose levels to prevent the occurrence of complications; and
2. The identification of pre-diabetes, to introduce annual re-testing for diabetes.

The economic evaluation considered two testing scenarios, denoted as:

- HbA1c\_1 (the base case scenario), where a single HbA1c cut-off is applied for the diagnosis of diabetes only; and
- HbA1c\_2 (the alternative scenario), where two diagnostic cut-offs are applied to enable a diagnosis of pre-diabetes and diabetes, respectively.

The limited clinical data presented in the application suggested that HbA1c testing may have similar performance to the current testing strategies at predicting diabetic retinopathy and therefore diabetes. If this data is accurate, then overall test accuracy is likely to be similar between the HbA1c\_2 test strategy – which includes pre-diabetes – and FPG with/without OGTT. However, the test accuracy in each testing, would be considerably lower than 100% and it is likely that different groups of patients within the spectrum of diabetes presentation, would be identified by each of the test strategies.

For the base case scenario, where an HbA1c cut-off was proposed to identify diabetes only, the intervention was observed to be less expensive, however is additionally, less effective than the current testing strategy. This was primarily due to the inability of HbA1c in this scenario to identify people with pre-diabetes.

From an economic perspective, the most economically efficient scenario would be that which identifies pre-diabetes and diabetes (the alternative scenario, HbA1c\_2), although the clinical uncertainty associated with this conclusion is significant. In the alternative analysis (HbA1c\_2), the intervention was dominant to the comparator testing strategy, as it is less costly for equivalent effectiveness. These differences were due to the ability (or inability) of the respective HbA1c testing strategies to identify pre-diabetes.

MSAC considered that the alternative economic evaluation scenario presented was more clinically relevant as it included HbA1c cut-off points for diabetes and pre-diabetes. Although MSAC noted that the results of the economic evaluation are highly uncertain due to the high degree of variability and comparisons made to imperfect reference standards. MSAC agreed that the gain in using HbA1c testing for diabetes and pre-diabetes was probably reasonable based on the estimated ICER for the alternative stepped scenario of \$4,421/QALY.

## **11. Financial/budgetary impacts**

The expected uptake of HbA1c testing for the diagnosis of diabetes was estimated in the application to range from 1.3-1.8 million tests for 1.1-1.4 million patients annually. However, there is substantial uncertainty in some inputs used to estimate these numbers, including GP administration of diabetes risk assessment, patient uptake of testing and test accuracy.

The total cost to the MBS for HbA1c testing was estimated in the application to range between cost savings of \$40 million to net costs of \$11 million annually<sup>1</sup>. Given the uncertainty in the estimated population eligible for testing, there is considerable uncertainty in the financial implications to the MBS.

MSAC agreed that the financial implications to the MBS were highly uncertain with estimates varying greatly between cost savings to net costs. MSAC noted that the uncertainties related to the size of the population eligible for testing and other parameters such as uptake of diabetes risk assessment and diagnostic testing, and recommendations for repeat testing in subsequent years. MSAC noted that if HbA1c testing is performed as part of a general health assessment including multiple pathology investigations, the additional cost of the HbA1c test to the MBS may be minimal due to cost coning when more than 3 tests are requested.

## **12. Other significant factors**

Nil.

## **13. Summary of consideration and rationale for MSAC's advice**

MSAC noted that HbA1c testing is currently reimbursed through the MBS (items 66551 and 66554) for the management of established diabetes to monitor effectiveness of treatment, whereas this application was seeking MBS listing for HbA1c testing for the diagnosis of diabetes mellitus (diabetes) in patients with undiagnosed diabetes who are considered at high

---

<sup>1</sup> Fact Correction – 18 June 2014: Figures corrected to be consistent with the published contracted assessment (CA) report (p145) and as presented and discussed by MSAC. The CA can be viewed at [www.msac.gov.au](http://www.msac.gov.au).

risk of the disease. MSAC considered that the creation of items for diagnostic purposes was unlikely to change the number of fasting blood glucose tests being requested opportunistically with other pathology tests.

MSAC agreed that determining potentially eligible patients who are at risk of diabetes using the AUSDRISK screening tool or according to NHMRC guidelines, as stated in the proposed descriptor, would be problematic. MSAC considered that the AUSDRISK screening tool was not an ideal method because of its poor sensitivity and that consideration of a patient's overall cardiovascular risk was better for case detection of diabetes. MSAC further noted that the descriptor of the comparators do not refer to the AUSDRISK score and was concerned that few General Practitioners currently use AUSDRISK as a screening tool. MSAC also discussed the merits of including a reference to include practice guidelines in the proposed descriptor and advised, in this instance, its preference for both to be excluded.

MSAC agreed that the two MBS listed blood glucose measures, fasting plasma glucose (FPG; item number 66500) test and the oral glucose tolerance test (OGTT; item number 66542) which are both recommended by Australian guidelines and routinely performed in Australia, were appropriate comparators. However, MSAC noted that although OGTT is considered the traditional gold standard, it is a flawed reference standard because of its high coefficient of variability (CV) compared to HbA1c testing (Diabetes Care February 2011). MSAC agreed that diagnosis of a diabetic complication such as retinopathy was a more objective reference standard against which to compare HbA1c testing for clinical effectiveness, safety and cost effectiveness.

Data from the DESIR study indicated similar performance (based on area under the ROC curve) for both FPG and HbA1c testing, while the DETECT-2 study indicated similar performance for OGTT, FPG and HbA1c in the general population. MSAC accepted that although the evidence presented demonstrated that the ability of all blood glucose measures to predict retinopathy was relatively poor, the performance of HbA1c testing was equivalent to FPG and OGTT. MSAC considered that there was merit in using the HbA1c test for diagnosing diabetes as it is at least as accurate as OGTT or FPG and is more convenient because there is no need for fasting beforehand. MSAC noted that three major international organisations have recommended HbA1c testing for diagnosis of diabetes on the basis of the strength of the relationship between it and retinopathy.

MSAC noted that the HbA1c test is already available and widely used in Australia for monitoring of diabetes and that it attracts the same or less risk than the comparators, therefore MSAC accepted that safety was not a concern for this assessment. MSAC noted the only risk was of misdiagnosis in haemoglobinopathies or red cell turnover disorders (thalassemias) but considered the risk to be minimal in NATA accredited laboratories where external quality assurance programs are in place.

MSAC considered that the alternative economic evaluation scenario presented was more clinically relevant as it included HbA1c cut-off points for diabetes and pre-diabetes. Although MSAC noted that the results of the economic evaluation are highly uncertain due to the high degree of variability and comparisons made to imperfect reference standards. MSAC agreed that the gain in using HbA1c testing for diabetes and pre-diabetes was probably reasonable based on the estimated ICER for the alternative stepped scenario of \$4,421/QALY. However, MSAC accepted that the model likely underestimated the benefits of HbA1c because it did not consider regression from pre-diabetes to normal due to lifestyle interventions.

MSAC agreed that the financial implications to the MBS were highly uncertain with estimates varying greatly between cost savings to net costs. MSAC noted that the

uncertainties related to the size of the population eligible for testing and other parameters such as uptake of diabetes risk assessment and diagnostic testing, and recommendations for repeat testing in subsequent years. MSAC noted that if HbA1c testing is performed as part of a general health assessment including multiple pathology investigations, the additional cost of the HbA1c test to the MBS may be minimal due to cost coning when more than 3 tests are requested.

MSAC was concerned about the ability to determine and monitor the number of tests for diagnosis of diabetes due to episode coning arrangements. A notional patient episode initiation (PEI) was suggested to allow monitoring of diabetes testing and it was also considered that data from the Medicine Insight program administered by NPS Medicinewise could be informative.

MSAC agreed there should be a limit on the frequency of testing, with the test in general available only once every 3 years to asymptomatic patients and limited to the smaller group of asymptomatic patients with additional indicators of concern to no more than once per person per year. MSAC considered a follow-up confirmatory test was unnecessary because measurement of HbA1c is more robust and reproducible than the existing blood glucose measures. MSAC suggested the limit be amended to read ‘no more than once per year and generally no more than 3 yearly’ for patients who are asymptomatic.

#### 14. MSAC’s advice to the Minister

After considering the strength of the available evidence in relation to the safety, effectiveness and cost-effectiveness of HbA1c testing for the diagnosis of diabetes, MSAC supported public funding of a new MBS item for quantitation of HbA1c for the diagnosis of diabetes in asymptomatic patients. MSAC did not support a confirmatory test to establish the diagnosis.

MSAC considered that the test in general should be offered once every 3 years to asymptomatic patients and limited to the smaller group of asymptomatic patients with additional indicators of concern to no more than once per person per year.

MSAC proposed descriptor:

Category 6 – Pathology Services Group P2- Chemical
MBS xxxxx
Quantitation of HbA1c (glycated haemoglobin) performed for the diagnosis of diabetes in asymptomatic patients at high risk.
Fee: \$16.80
Limit: Not more than one per person per year and generally no more than every third year.

#### 15. Applicant’s comments on MSAC’s Outcomes

Our committee would like to thank the MSAC for their positive recommendation for the use of the HbA1c (glycated haemoglobin) for the diagnosis of diabetes. Although not ideal and not consistent with current guidelines, the committee notes the decision of MSAC to only require one test for the diagnosis of diabetes. The committee believes an education program will allow for the appropriate use of subsequent Medicare-funded investigations to confirm and manage diabetes after a single diagnostic test. There are a couple of minor points that the committee would like to emphasise. Firstly, we disagree with MSAC with regard to the AUSDRISK score. It does not have poor sensitivity and should continue to be the preferred screening tool; cardiovascular disease risk does not have better sensitivity. Secondly, the



wording of the descriptor contains some imprecise wording which may create difficulties regarding audit compliance if used for this purpose. The committee believes that the approval must be for 1 test per year for diagnosis to simplify audit processes. However, member organisations of our committee will undertake an educational program that will address issues such as who represents high risk patients needing to be tested as frequently as once per year and which patients may be at lower risk "generally" needing a test only once every three years. Finally, high quality control systems in NATA accredited laboratories will still not overcome all issues pertaining to the impact of haemoglobinopathies and reduced red blood cell survival time on the glycated haemoglobin level where glucose based testing remains preferred. Once again, an on-going education program undertaken by our professional organisations will hopefully minimise this small risk.

## **16. Linkages to other documents**

Further information is available on the MSAC Website at: [www.msac.gov.au](http://www.msac.gov.au).