



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1146.1 – Capsule Endoscopy for the Diagnosis of Suspected Small Bowel Crohn Disease

Sponsor/Applicant/s: Given Imaging Pty Ltd

Date of MSAC meeting: 28 November 2013

1. Purpose of application

The resubmission was submitted by Given Imaging on 12 June 2013 to the Department of Health.

Capsule endoscopy (CE) is a non-invasive diagnostic test, usually conducted in an outpatient setting, in which the gastrointestinal system is visualised via a camera inside an ingested capsule. The test visualises the gastrointestinal tract mucosa to diagnose a range of conditions such as obscure gastrointestinal bleeding (OGIB), coeliac disease, small bowel tumours and Peutz-Jeghers syndrome.

CE is currently funded through the MBS for two indications:

- for the investigation of OGIB (MBS item 11820); and
- for the conduct of small bowel surveillance of a patient with Peutz-Jeghers syndrome (MBS item number 11823).

CE for investigation of OGIB originally received interim MBS funding following consideration by MSAC in 2003 (Application 1057). MSAC reconsidered this indication in 2007 with MSAC recommending full MBS listing. The use of CE for Peutz-Jeghers syndrome was considered by MSAC in 2007 (Application 1119).

Crohn disease is a chronic inflammatory bowel disease that may affect any portion of the gastrointestinal tract but, in cases of small bowel involvement, typically affects the terminal ileum. Most patients with isolated small bowel Crohn disease are diagnosed using colonoscopy with ileoscopy; however diagnosis can be difficult due to the inaccessibility of the small bowel.

2. Background

At the July 2011 meeting, MSAC did not support public funding of CE to evaluate suspected small bowel Crohn disease (Application 1146), in patients who have had some previous testing which remains inconclusive, after considering the strength of the available evidence in relation to the safety, effectiveness and cost-effectiveness.

MSAC concluded that CE had *prima facie* clinical utility, but there were substantial deficiencies with the evidence base around comparative safety, accuracy and clinical effectiveness data for CE relative to alternative ways of investigating patients with suspected small bowel Crohn disease. MSAC also observed that it had to assume that the four existing capsule endoscopic technologies are the same, even though it had no evidence to support this assumption.

3. Prerequisites to implementation of any funding advice

The capsules (PillCam^RSB, MiRo-Cam, EndoSapsule and CapsoVision) are TGA approved; there are no specific conditions on its TGA certification.

This application specifically deals with PillCam^RSB CE.

CE is usually performed in an outpatient setting. Consistent with other MBS listings of CE, it is presumed that any CE service will only attract a MBS benefit when performed by a specialist or consultant physician with endoscopic training recognised by The Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy (and Medicare Australia is notified of that recognition).

4. Proposal for public funding

Applicant Proposed MBS item descriptor

Category 2 – Diagnostic procedures and investigations	
MBS TBD	
CAPSULE ENDOSCOPY to diagnose suspected Crohn disease, using a capsule endoscopy device approved by the Therapeutic Goods Administration (including administration of the capsule, imaging, image reading and interpretation, and all attendances for providing the service on the day the capsule is administered), if:	
(a) The patient to whom the service is provided :	
i. is aged 2 years over; and	
ii. has not been previously diagnosed with Crohn disease	
iii. has suspected Crohn disease on the basis of evidence of underlying inflammation, as indicated by elevated Erythrocyte Sedimentation Rate and/or C-Reactive Protein or other inflammatory markers; and	
(b) The service is performed by a specialist or consultant physician with endoscopic training that is recognised by The Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy; and	
(c) Prior negative colonoscopy with attempted ileoscopy has been performed on the patient, and has not produced a confirmed positive or negative diagnosis of Crohn disease; and	
(d) Prior radiographic imaging has been performed on the patient, and has not produced a confirmed positive or negative diagnosis of Crohn disease or evidence of strictures. Radiographic diagnostic procedures previously used by the patient may include:	
iv. magnetic resonance enterography (MRE), or	
v. computed tomography enterography (CTE), or	
vi. small bowel follow through (SBFT) testing, and	
(e) the service is not associated with balloon enteroscopy; and	

(f) the service has not been provided to the same patient on more than 2 occasions in any 12 month period.

This item is not for use by patients previously diagnosed with Crohn disease

Fee: \$2,039.20 Benefit: 75% = \$1,529.40 85% = \$1,964.70

Conjoint committee

The Conjoint Committee comprises representatives from the Gastroenterological Society of Australia (GESA), the Royal Australasian College of Physicians (RACP) and the Royal Australasian College of Surgeons (RACS). For the purposes of Item TBD, specialists or consultant physicians performing this procedure must have endoscopic training recognised by The Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy, and Medicare Australia notified of that recognition.

CE would be restricted to patients with suspected but unconfirmed small bowel Crohn disease, as indicated by ongoing symptoms suggestive of Crohn disease such as abdominal pain, diarrhoea, extra intestinal symptoms or raised inflammatory markers on blood tests.

Patients who are eligible for CE would have undergone prior endoscopy or radiographic imaging and not have received a confirmed positive diagnosis for Crohn disease or have evidence of strictures.

CE to diagnose suspected Crohn disease would be performed by a specialist or consultant physician with endoscopic training recognised by The Conjoint Committee for the Recognition of Training in Gastrointestinal Endoscopy (and Medicare Australia is notified of that recognition).

5. Consumer Impact Statement

Feedback was received from two professional bodies on the consultation Protocol regarding the impact on consumers.

For consumers, the advantage of CE was that it reduces the risk of an incorrect diagnosis of Crohn disease in patients where conventional means are unclear. Consumers gained greater confidence in the potential efficacy of immunosuppressive therapy and the knowledge that potential risks associated with such therapy were justified.

Disadvantages were minimal, although it was noted that the main concern with CE is the risk of capsule retention.

It was stated that current access is inequitable. The service is currently provided to patients able to privately fund the procedure, those that have a private insurer willing to subsidise the procedure or in those attending a public institution which bears the cost of the procedure.

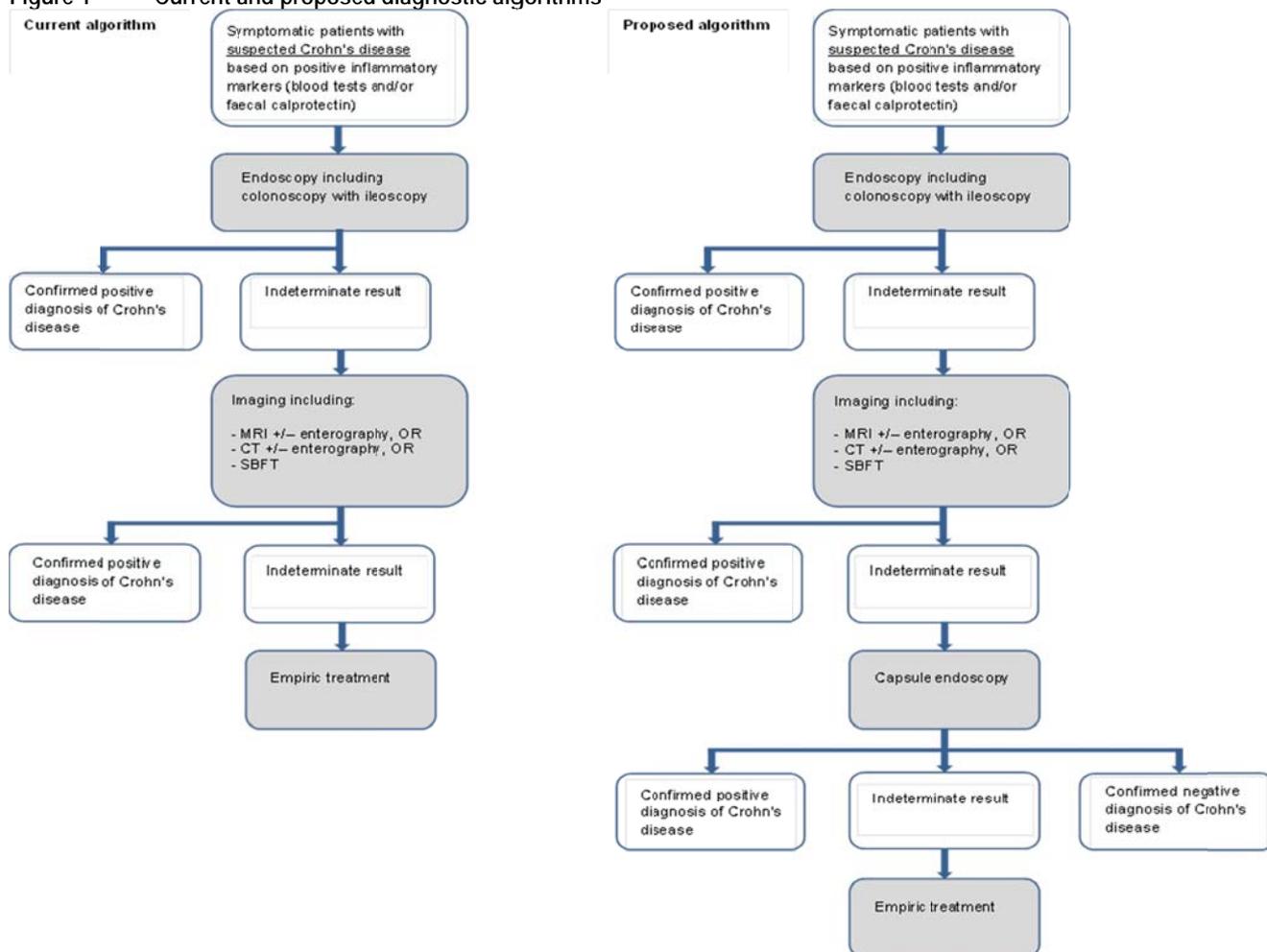
6. Proposed intervention's place in clinical management

The clinical management algorithm proposed in the resubmission differed to that from the previous MSAC application (1146), in that it clearly specified that CE should be positioned after endoscopy and small bowel radiology. Under the current diagnostic algorithm for Crohn disease, if a patient still has unconfirmed disease after going through endoscopic and radiographic testing, the only option currently available to patients is empiric treatment.

The proposed treatment algorithm included an extra step for CE prior to empiric treatment. CE is able to visualise areas of the proximal small bowel inaccessible to upper and lower endoscopy; which may lead to earlier diagnosis and treatment. In the proposed diagnostic flow chart (below) CE would be positioned after computed tomography enterography (CTE), magnetic resonance enterography (MRE) or small bowel follow through (SBFT), and will replace empiric treatment based on a suspicion of Crohn disease which could not be

confirmed. The resubmission proposed that CE should be regarded as a last-line approach to diagnosis, for use in patients who cannot be diagnosed through using other tests.

Figure 1 Current and proposed diagnostic algorithms



7. Other options for MSAC consideration

Nil

8. Comparator to the proposed intervention

The Protocol stated that the main comparator for CE is empiric treatment as patients who receive CE will have already undergone small bowel imaging with CTE, MRE or SBFT. The comparator in this case is not a traditional diagnostic test but rather long term 'treatment response' over a 12 month period that is seen as a surrogate for a diagnosis of Crohn disease in the comparator arm.

According to the resubmission, very few patients who commence empiric treatment (in a world without CE) would have their diagnosis reclassified in this 12 month time horizon. In the comparator arm, at the beginning of treatment patients were assumed to have a 'working (but not a confirmatory) diagnosis of Crohn disease. It was also assumed that a subsequent clinical response to treatment must mean the underlying diagnosis is Crohn disease.

MSAC agreed with the resubmission that, in the absence of CE after failure to make a definite diagnosis of Crohn disease after endoscopy and radiographic imaging, the appropriate comparator is empiric Crohn disease therapy (immunosuppressants such as azathioprine, 6-mercaptopurine or methotrexate and tapering doses of corticosteroids).

However, MSAC noted that, in practice, some patients may be observed and not treated rather than treated empirically, especially those with milder symptoms.

8. Comparative safety

The Protocol proposed that the resubmission further address the issue of overstated risk of capsule retention, noting the following:

- patients who are eligible for CE will have already undergone CTE or MRE, both of which can be used to identify strictures; and
- in patients who are suspected of having strictures, Pillcam® SB comes with a dissolvable capsule (Agile™) to test the patency of the gastrointestinal tract before CE.

The resubmission stated:

- the primary basis for MSAC concerns in 2011 around safety was predominantly based on a single study (Ge et al 2004) that reported a capsule retention rate of 15% and that the risk of retention was overstated;
- the ‘updated literature’ on retention data which has been refined to take into account the new eligible population where patients at high risk of retention have been excluded; and
- that across the 6 included studies (Table 1) examining retention in 303 patients there was a retention rate of 4%, and of the listed studies, the study by Selby (2008) (which reported a retention rate of 0.8%) was in an Australian population

No new safety data was included from that considered by MSAC in 2011. The resubmission identified six studies that were applicable for the proposed eligible patient population. The diagnostic yield study of Selby (2008) was cited as the most applicable in terms of safety as it was generated in the Australian health care setting.

MSAC agreed that the rate of capsule retention was likely to be less than the 15% the committee had emphasised previously, but the assumed CE retention rate of 1% in the model was at the low end of the range of estimates from across all the studies provided.

Table 1: Adverse events from CE in suspected Crohn disease

Study	Retention		Surgery following retention	
	n/N	% (95% CI)	n/N	%
Figuerdo 2010	4/78	5.1% (1.6%-12.9%)	2/4	50%
Girelli 2007	3/27	11.1% (3.0%-28.9%)	2/3	66.7%
Selby, 2008	1/120	0% (0%-5.0%)	NR	
Eliakim, 2004	0/35	0% (0%-11.8%)	N/A	
Ge, 2004	3/20	15% (4.4%-36.9%)	NR	
Valle, 2006	2/23	8.7% (1%-28.0%)	1/2	50%

MSAC had previous concerns around the predictive accuracy of prior tests to identify strictures that place patients at high risk of capsule retention. However, PASC noted that the risk of capsule retention was low, as patients with small bowel strictures would have been

excluded based on prior imaging. If capsule retention occurs, the capsule would be removed surgically or by balloon enteroscopy.

In patients who are suspected of having strictures, Pillcam[®] SB comes with a dissolvable capsule (Agile[™]) to test the patency of the gastrointestinal tract before CE. However, no studies were presented to confirm a reduced incidence of capsule retention when Agile[™] is used.

It is not clear whether other branded capsules on the Australian market have an accompanying patency capsule to inform whether a patient is at risk of retention.

MSAC noted that the Protocol proposed that in instances of technical failure, the applicant would provide an extra capsule, free of charge under the standard warranty terms. If the Pillcam[®] SB is unable to adequately visualise the small bowel for other reasons, this would be picked up in studies of diagnostic accuracy and accounted for in the economic evaluation. PASC considered that technical failure rates were likely to be low but that a technical failure would result in a second Medicare claim for a repeat CE procedure.

On balance, MSAC concluded that CE is safer than empiric Crohn disease treatment for the proposed population without confirmed Crohn disease.

10. Comparative effectiveness

The Protocol proposed that the resubmission present, if available, direct evidence for the impact of CE on health outcomes. In the absence of direct evidence, the resubmission should present indirect evidence indicating the impact of CE on clinical management and patient outcomes.

The resubmission identified primary evidence on CE most likely to be relevant for the proposed patient population; however the resubmission also reiterated the broader evidence base around CE regardless of its applicability. The resubmission also graded the applicability of each primary study against research questions outlined in the protocol.

No direct evidence of the effect on health outcomes was identified in terms of the incremental value of adding CE (versus not) at this point in the patient pathway. Of the primary studies that were identified, the majority were in relation to diagnostic performance with one study looking at change in patient management. The systematic reviews that were referred to appeared to have poor applicability (which was also the conclusion of the resubmission). The resubmission primarily presented accuracy data of the ‘capsule arm’ where there was a comparison between the capsule and the reference standard within this arm of the protocol.

In relation to the reference standard, the Protocol identified this as ‘follow up at 12 months’. Of the three accuracy studies considered most applicable to the resubmission’s proposed patient population, each had slightly different time horizons for their reference standard. For Figueiredo (2010) the reference standard was diagnosis at follow-up (>6 months), based on contact with the referring physician; for Girelli (2007) the reference standard was final diagnosis after long-term follow-up (median 21 months), including histological confirmation of surgical and enteroscopic tissue samples when available; and for Tukey (2009) the reference standard was diagnosis at 12 months, including radiological, histological or endoscopic abnormalities consistent with Crohn disease or treatment for Crohn disease on the basis of symptoms and additional objective findings.

The resubmission's clinical claim was that CE will identify a subgroup of tested patients for whom a diagnosis of Crohn disease is excluded and therefore these patients will avoid inappropriate treatment.

MSAC agreed with the Protocol that the negative predictive value (NPV) of CE should be the key measure of diagnostic performance. The NPV (probability of no disease if a person has a negative test result) is of practical clinical value in making decisions to either discontinue treatment or a decision of "no treatment" (i.e. it is a measure of clinical validity). However, predictive values cannot readily be transferred to different populations or easily pooled to produce a summary estimate.

The resubmission pooled the predictive values for the studies with high applicability, that is, studies which contained a subgroup of patients with negative or equivocal results on prior testing. The pooled NPV was 77% (95% CI: 70%-85%) and the pooled PPV was 92% (95% CI: 84%-100%).

The reported prevalence of Crohn disease in Figueiredo (2010), Girelli (2007) and Tukey (2009) was 43%, 50% and 13% respectively. In the subgroup of patients who received prior small bowel radiology, the prevalence of Crohn disease in each of these studies was calculated as 51%, 56% and 13% respectively. Calculation of prevalence includes false negatives (in addition to true positives) in the numerator therefore there is a small proportion of prevalent cases of Crohn disease not picked up by CE and miss out on beneficial treatment. However, false negatives make up only a small proportion of the numerator and as the prevalence goes up from 13% to over 50% in the three included studies, the NPV of CE (although decreasing as predicted as prevalence increases), holds reasonably well above 90% (91% only down from 97%).

In relation to analytical validity, the resubmission showed that CE had better sensitivity than specificity. The pooled results from the three most relevant accuracy studies showed an overall sensitivity of 92% (95% CI: 81%-98%) and specificity of 77% (95% CI: 60% - 79%).

Overall, MSAC concluded that, for patients who have had multiple prior investigations, a negative CE result would exclude the possibility of Crohn disease with a reasonable level of confidence.

11. Economic evaluation

Consistent with the Protocol, the resubmission presented a cost-effectiveness analysis based on a superiority claim and a modelled economic evaluation to translate the diagnostic accuracy/effectiveness data into final patient outcomes (quality-adjusted life years, QALYs). Consistent with the previous MSAC assessment report, a healthcare system perspective was used, including the cost to the government and cost to the patient.

The Protocol also proposed that patients in whom there remains clinical suspicion of Crohn disease but who have received inconclusive results from prior endoscopy and radiography are treated under the assumption that they have Crohn disease in a world without CE. It was assumed in the subsequent economic analysis that all patients in the "no CE" comparator group will commence empirical treatment for Crohn disease and that the incremental value of CE is that a proportion of patients who truly do not have Crohn disease will avoid treatment for Crohn disease because of the diagnostic properties of CE. Consistent with the Protocol, which referred to the published economic evaluation by Levesque et al (2010), patients who have bowel disease other than Crohn disease are assumed to have irritable bowel syndrome (IBS).

The resubmission presented a one year cost-effectiveness analysis, which modelled the additional diagnostic value offered by CE when compared with no CE. CE was shown to affect the proportion of patients who received a confirmed diagnosis, thereby improving effectiveness of downstream disease management. The improved effectiveness was translated into the number of QALYs as well as potential cost savings associated with preventing costly Crohn disease treatment from being given to patients who in fact do not suffer from the condition.

The base case economic evaluation estimated an incremental cost per extra QALY gained of \$23,672. A number of sensitivity analyses were presented which showed that when an assumption was varied (univariate analysis) based on the uncertainties in the cost input and clinical/epidemiological variables, the resultant ICERs ranged mostly between \$20,000 and \$30,000. The resubmission report did not present any multi-way sensitivity analyses. ESC considered that there may be some value in performing multi-way sensitivity analyses based on utility scores and cost of treatment in the comparator arm.

The resubmission considered the lower prevalence generated in the Tukey (2009) study as well as the low estimated prevalence calculated from diagnostic yield studies such as Selby (2008) relevant to inform the base case of the economic model. According to the resubmission, the increased sensitivity in prior testing was likely to decrease the prevalence of true Crohn disease in the tested population and that the underlying evidence base has the potential to overestimate prevalence as the primary studies predominantly used SBFT (versus CTE/MRE). The resubmission also stated that high baseline prevalence may not make the addition of CE a cost-effective strategy because 'empiric treatment' would in fact represent a correct and effective treatment for the underlying Crohn disease and thus provide a QALY gain in many patients.

MSAC considered that the main area of economic uncertainty was the appropriateness of the utility weights as the ICER is highly sensitive to the difference in utility weights, and that this issue should be further explored to ensure the assigned scores reflect the best available evidence.

MSAC also considered that the following issues with the economic evaluation, which were identified by ESC, should be addressed in a future submission:

- the assumed prevalence may have been biased towards CE because it resulted in patients in the empiric treatment arm not accruing any utility gain during the time horizon of the model;
- the assumption that all therapy lasted the full 12 months' time horizon of the model irrespective of response which seemed clinically implausible;
- the assumption that all patients without a clear diagnosis after both endoscopy and radiographic imaging would receive empiric Crohn disease therapy was not supported with evidence; and
- the 12-month time horizon of the model may have biased against CE by excluding surgery cost offsets and later cost offsets.

12. Financial/budgetary impacts

The number of CE procedures was estimated to be between 714 and 1,538 per year.

The proposed MBS schedule fee for CE is \$2,039.20. This is the same as CE for obscure gastrointestinal bleeding (item 11820) and for Peutz-Jeghers syndrome (item 11823).

The net financial costs of the new service were estimated to be \$1.5–3.2 million/year, based on estimates of the incidence of Crohn disease, the number of Crohn disease cases diagnosed by CE and the diagnostic yield in the eligible population. MSAC was concerned that this may be underestimated.

13. Other significant factors

Issues with the descriptor

ESC agreed that small bowel should be included in the descriptor despite being excluded in the proposed descriptor suggested by the resubmission. ESC also questioned whether the descriptor should include the words ‘not associated with balloon enteroscopy’. The Department suggested removal from the descriptor of “approved by the Therapeutic Goods Administration” as legislatively a product cannot be used on a person if it is not TGA approved.

At the MSAC 59th meeting on 1 August 2013, MSAC recommended for Application 1346 (amendments to MBS item 11820):

- removal of:
 - a. age restriction;
 - b. the services is not associated with double balloon; and
 - c. the time restriction for the service - that requires the CE procedure to be performed within six months of the upper gastrointestinal endoscopy and the colonoscopy which did not identify the cause of the gastrointestinal bleeding.
- inclusion of:
 - a. associated endoscopy procedure if required for placement after (including administration of the capsule).
- MSAC also noted that since CE was first listed on the MBS, the unit cost of the capsule has dropped and therefore the price of the capsule which is included in the fee should be reviewed. This item should also be removed from standard indexation of MBS items.

The Department suggested that these proposed descriptor changes for MBS item 11820 should also apply to the descriptor in this application.

Capsule cost

Concerns were expressed regarding the cost of the capsule, particularly as an article from 17 June 2013 from the Israeli Foreign Trade Administration stated that Given Imaging, Israeli Manufacturer, seeking FDA Approval for PillCam Colon capsule will sell for approximately US \$500, similar to the price of a PillCam SB capsule.

Similar to MBS Item 11820, the proposed listing for CE to evaluate suspected small bowel Crohn disease would be one of very few items in the MBS which included the cost of a device and capital costs. Unlike many devices, the device does not meet the eligibility criteria for listing as a prosthesis, meaning its cost is not required to be met by private health insurance.

Incorporating the cost into the Medicare benefit enables some or all of the cost of the device to be covered. Therefore, a higher amount for this service is paid than would be the case if the item descriptor only covered the professional service.

14. Key issues for MSAC from ESC

ESC considered that the ICER of \$23,672/QALY could not be relied upon, as the structure of

the model did not compare clinically plausible scenarios and the assumptions used in the model tend to favour CE.

15. Summary of consideration and rationale for MSAC's advice

The July 2011 MSAC meeting did not support public funding of capsule endoscopy (CE) to evaluate suspected small bowel Crohn disease (CD) (application 1146) in patients who have had some previous testing which remains inconclusive. That decision was based on the applicant's failure to demonstrate superior comparative diagnostic accuracy or improved health outcomes and acceptable cost-effectiveness, as well as the potential for wider use of CE to diagnose other suspected gastrointestinal conditions. The applicant resubmitted the application for CE identifying a residual unmet clinical need for a subgroup of patients (5%) with suspected CD, who are defined as having underlying evidence of inflammation, but no definite diagnosis despite prior investigations, firstly with colonoscopy with attempted ileoscopy, and secondly with radiographic imaging such as magnetic resonance enterography (MRE), computerised tomography enterography (CTE), or small bowel follow through (SBFT). MSAC noted that the target population could be more rigorously defined, for example by specifying thresholds for the systemic inflammation markers of elevated erythrocyte sedimentation rate and C-reactive protein.

MSAC agreed with the resubmission that, in the absence of CE after failure to make a definite diagnosis of CD after endoscopy and radiographic imaging, the appropriate comparator is empiric CD therapy (immunosuppressants such as azathioprine, 6-mercaptopurine or methotrexate and tapering doses of corticosteroids). However, MSAC noted that, in practice, some patients may be observed and not treated rather than treated empirically, especially those with milder symptoms. At the beginning of CD treatment, the resubmission assumed that patients would have a 'working' (but not a confirmed) diagnosis of CD. The resubmission also assumed that a subsequent clinical response to empiric CD treatment would confirm that the underlying diagnosis is CD.

The resubmission argued that the risk of capsule retention due to strictures was overstated in the previous assessment report and identified six studies that are applicable for the eligible population under consideration. Selby (2008), which reported a retention rate of 0.8%, was cited as the most applicable as it was generated in the Australian healthcare setting. MSAC agreed that the rate of capsule retention was likely to be less than the 15% the committee had emphasised previously, but the assumed CE retention rate of 1% in the model was at the low end of the range of estimates from across all the studies provided. In patients who are suspected of having strictures, Pillcam[®] SB comes with a dissolvable capsule (Agile[™]) to test the patency of the gastrointestinal tract before CE. However, no studies were presented to confirm a reduced incidence of capsule retention when Agile[™] is used. On balance, MSAC concluded that CE is safer than empiric CD treatment for the proposed population without confirmed CD.

Diagnostic accuracy in patients with prior negative or equivocal tests for CD showed CE had better sensitivity than specificity. The pooled results from the three most relevant accuracy studies showed an overall sensitivity of 92% and specificity of 77% using clinical follow-up at 6 months, 12 months or to a median of 21 months as the reference standard. The diagnostic yield was 29–54% (29% in Selby (2008)). MSAC questioned what happens to patients with negative CE findings when considering that only one low-quality study documented any change in clinical management and so a linked evidence approach was required.

MSAC examined the clinical claim that a negative CE result would confidently exclude CD in a subgroup of patients (and thus those patients would then get appropriate non-CD

treatment and avoid inappropriate CD treatment). According to the protocol finalised by PASC, the negative predictive value (NPV) (the probability of no disease if a person has a negative test result) of CE should be the key measure of diagnostic performance. In this small target population where the baseline prevalence tends to decrease, the NPV tends to increase. NPV cannot readily be transferred to different populations or easily pooled to produce an overall estimate, but the estimates from the three studies presented ranged between 91% and 97%. Overall, MSAC concluded that, for patients who have had multiple prior investigations, a negative CE result would exclude the possibility of CD with a reasonable level of confidence.

When considering the economic evaluation, MSAC was primarily concerned about the arbitrary nature of the utility weights for correctly diagnosed and treated disease (0.766) and for incorrectly diagnosed and treated disease (0.68). The application's utility estimates were the same regardless of whether the disease was CD or irritable bowel syndrome (IBS), the alternative diagnosis for these patients. The utilities were also inconsistent with those of Levesque *et al.* (2010), in which the difference between these utility weights was less (0.02). Although Levesque *et al.* (2010) had been cited by PASC and ESC as a potentially informative economic evaluation conducted in the United States addressing similar questions, the applicant's Pre-MSAC Response attempted to dismiss it, arguing that the study assessed patients with less severe symptoms than the proposed target population. However, MSAC commented that the comparison examining the inclusion of CE in the Levesque *et al.* (2010) paper also related to its use as a third test in patients for whom a high suspicion of disease remains after two previous negative tests.

MSAC noted that leaving all other aspects of the economic evaluation unchanged and replacing the submission's estimate of the utility difference between successful and unsuccessful treatment with the estimate from Levesque *et al.* (2010) would increase the incremental cost per extra quality-adjusted life-year gained from \$23,672 to \$115,903.

MSAC queried why the utility would improve with symptomatic treatments for IBS given that these medicines would have been trialled previously and those responding would have been eliminated from this arm. The sensitivity analyses did not test variation in utility for correct diagnosis of IBS. As the utility gain for CE in the model was mostly determined by IBS patients avoiding ineffective CD medicines used to treat a condition they do not have, MSAC agreed that the model was biased in favour of CE.

MSAC noted the other following matters with the economic evaluation which were not all addressed by the applicant's Pre-MSAC Response even though they were identified by ESC:

- the assumed prevalence of 13% may have been biased towards CE because it resulted in 87% of patients in the empiric treatment arm not accruing any utility gain during the time horizon of the model – MSAC noted (a) the sensitivity of the model to this parameter, and (b) the fact that the other two studies estimated prevalence in these patients as 51% and 56% reflected a high index of suspicion by the treating clinician sufficient to warrant further investigation in this patient group;
- the assumption that all therapy lasted the full 12 months' time horizon of the model irrespective of response which seemed clinically implausible – MSAC considered that this (a) was biased towards CE in the empiric treatment arm because the costs of CD treatment were applied for all patients for the full 12 months, but utility gains only accrued for the 13% with CD based on the assumed prevalence; and (b) may have been biased to a lesser extent against CE in the CE arm because the estimated cost per patient of IBS treatment is less than the estimated cost per patient of CD treatment;

- the assumption that all patients without a clear diagnosis after both endoscopy and radiographic imaging would receive empiric CD therapy was not supported with evidence;
- the 12-month time horizon of the model may have biased against CE by excluding surgery cost offsets and later cost offsets.

MSAC commented that its considerations regarding the fee had not changed since its previous appraisal of CE in August 2013.

MSAC noted that the net financial costs of the new service are \$1.5–3.2M/year, based on estimates of the incidence of CD, the number of CD cases diagnosed by CE and the diagnostic yield in the eligible population. MSAC raised a concern that these may be underestimates because of the risks of wider usage to diagnose other gastrointestinal conditions and of repeat uses of CE in a patient for surveillance or monitoring purposes.

In conclusion, MSAC accepted that CE appears safe and sufficiently diagnostically accurate in the investigation of these patients, with an expected improvement in subsequent clinical management, but did not accept the economic evaluation presented a sufficiently robust basis to determine its cost-effectiveness.

Lay summary

Capsule endoscopy is a way to record images of the gastrointestinal tract. The capsule is the size and shape of a pill and contains a tiny camera. Capsule endoscopy is generally used to examine areas of the small intestine that cannot be seen by other types of endoscopy.

The applicant has resubmitted an application for capsule endoscopy (CE) to evaluate suspected small bowel Crohn disease (CD) in patients with an unconfirmed diagnosis despite multiple prior investigations. This intervention was compared against using medicines for CD in patients with unconfirmed disease, who may have other causes for their symptoms.

MSAC accepted that CE appears safe and sufficiently diagnostically accurate in the investigation of these patients but did not accept the economic evaluation presented. Therefore, MSAC did not support public funding and suggested that the applicant review the assumptions proposed in the economic evaluation.

16. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to the safety, clinical effectiveness and cost-effectiveness of capsule endoscopy to evaluate suspected small bowel Crohn disease in patients who have had both endoscopic and radiographic imaging which remains inconclusive, MSAC does not support its public funding.

17. Applicant's comments on MSAC's Public Summary Document

No comment.

18. Context for decision

This advice was made under the MSAC Terms of Reference.

MSAC is to:

Advise the Minister for Health on medical services that involve new or emerging technologies and procedures and, where relevant, amendment to existing MBS items, in relation to:

- the strength of evidence in relation to the comparative safety, effectiveness, cost-effectiveness and total cost of the medical service;
- whether public funding should be supported for the medical service and, if so, the circumstances under which public funding should be supported;
- the proposed Medicare Benefits Schedule (MBS) item descriptor and fee for the service where funding through the MBS is supported;
- the circumstances, where there is uncertainty in relation to the clinical or cost-effectiveness of a service, under which interim public funding of a service should be supported for a specified period, during which defined data collections under agreed clinical protocols would be collected to inform a re-assessment of the service by MSAC at the conclusion of that period;
- other matters related to the public funding of health services referred by the Minister.

Advise the Australian Health Ministers' Advisory Council (AHMAC) on health technology assessments referred under AHMAC arrangements.

MSAC may also establish sub-committees to assist MSAC to effectively undertake its role. MSAC may delegate some of its functions to its Executive sub-committee.

19. Linkages to other documents

MSAC's processes are detailed on the MSAC Website at: www.msac.gov.au.