



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1515 Endoscopic placement and removal of an intragastric balloon for the management of moderate obesity in patients with type 2 diabetes mellitus who have failed first-line treatments

Applicant: Apollo Endosurgery Australia

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](#)

1. Purpose of application

An application requesting Medicare Benefits Schedule (MBS) listing of the endoscopic placement and removal of an intragastric balloon (IGB) for the treatment of patients aged ≥ 18 years with moderate obesity (body mass index (BMI) of 30.0 to 34.9 kg/m²), who have poorly controlled type 2 diabetes mellitus (T2DM) and who have failed first-line treatment options, was received from Apollo Endosurgery Australia by the Department of Health.

2. 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 did not support public funding for endoscopic placement and removal of an IGB for the management of moderate obesity in patients with poorly controlled T2DM who have failed first-line treatments. MSAC considered that IGB had inferior safety (relative to lifestyle interventions) and noted the recent safety concerns (e.g. Therapeutic Goods Administration [TGA]) with use of IGB in clinical practice. MSAC considered the clinical effectiveness evidence was highly uncertain, particularly over the long-term after removal of the device, and that these uncertainties flowed to the economic analysis.

Consumer summary

Apollo Endosurgery Australia applied for public funding via the Medicare Benefits Schedule (MBS) for the procedure to insert an intragastric balloon in people who have type 2 diabetes *and* who have been assessed as having moderate obesity (body mass index (BMI) of 30.0–34.9) *and* who have not responded to other 'first line' treatments, such as weight-loss medicines and lifestyle changes.

Consumer summary

An intragastric balloon (IGB) is a small silicon balloon that is inserted into a patient's stomach using an endoscopic procedure (that is, a tube placed down the throat and into the stomach). A doctor fills the balloon with saline solution to create a feeling of fullness, so patients lose the urge to overeat, and thus lose weight. The balloon is removed after 6 or 12 months.

MSAC acknowledges the need to help patients manage diabetes and to support patients who are significantly overweight to reduce weight. However, there are a number of safety concerns with the use of these balloons. Many people who have used this device in clinical trials have reported serious side effects and there have also been some deaths reported. In addition, there is limited clinical evidence of the effectiveness of this device. The evidence available shows that, while patients can lose weight initially, most of the weight is regained within 12 months of the balloon being removed.

MSAC's recommendation to the Commonwealth Health Minister

MSAC did not support public funding for endoscopic placement and removal of an IGB for the management of moderate obesity in patients with poorly controlled type 2 diabetes mellitus who have failed first-line treatments. This is because MSAC is concerned about the effectiveness and safety of the IGB. The economic evaluation and financial impact presented in the application was also highly uncertain.

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

Application 1515 requests MBS listing of the endoscopic placement and removal of an IGB for the treatment of patients aged ≥ 18 years with a BMI of 30.0–34.9 kg/m² who have poorly controlled type 2 diabetes mellitus (T2DM) and who have failed first-line treatment options. MSAC noted that this range of BMIs was chosen because these patients are not eligible for bariatric surgery.

MSAC noted that there was only a low level of clinical evidence available. In the past 20 years, only two randomised controlled trials (RCTs) have been published, and they were open label, with short durations of follow-up and small sample sizes, and a high risk of bias. Observational studies show a better effect than the clinical trials, but this level of evidence is not sufficient for MSAC's purposes. MSAC noted that there are five clinical trials currently in progress.

MSAC noted that the application differed from the ratified PICO; the population, intervention and comparator were changed in the assessment. The applicant presented a cost-consequence analysis in addition to the cost-utility analysis.

MSAC noted that the clinical effectiveness is not sustained beyond 12 months. Patients who undergo IGB need to have at least 10% weight loss to achieve positive outcomes. The meta-analysis results from the two RCTs on weight loss outcomes significantly favoured IGB plus lifestyle over lifestyle alone. However, weight regain from 6 to 12 months post-removal of the IGB was substantial in both studies. The effect size of the weight loss outcomes was consistently smaller at 12 months than at 6 months. Given that the follow-up period is only for 12 months, it is uncertain what the effectiveness of the IGB plus lifestyle intervention is in the long term. There is a lack of RCT or high-quality observational evidence to support effectiveness beyond 12 months.

MSAC noted significant safety issues. MSAC noted that both the US Food and Drug Administration (FDA) and the TGA reported deaths from the use of IGBs. In the Courcoulas 2017 and Fuller 2013 trials (total of 191 patients), 98% of the patients reported adverse events (AEs). MSAC noted that the IGB was removed from some patients within 6 months in both trials due to serious procedure-related and device-related AEs.

MSAC noted that the incremental cost-effectiveness ratio (ICER) is highly uncertain, varying from ~\$redacted in the trial-based analysis to ~\$redacted in the modelled base-case analysis. The range of ICERs reflects the uncertainty of the duration of treatment effect of IGB on weight loss and T2DM. MSAC also noted that the economic model did not include the disutility associated with AEs (although these were common, they were assumed to not incur any cost). This could be a major concern, as the disutility associated with the early removal may be high, and weight loss and quality of life benefits may not be achieved for these patients.

MSAC noted that the financial impact was also highly uncertain as the proportion of eligible patients expected to receive an IGB was based on current uptake of bariatric surgery. The financial impact could be profoundly affected if the proposed MBS item descriptor applies to the 4.25 million obese patients in Australia.

MSAC noted the negative feedback that some consumers have reported about the IGB. Consumers also reported that people who undergo this procedure need support and counselling to change their eating and lifestyle habits, not just insertion of the IGB alone. MSAC noted that IGBs could be used as a bridge to bariatric surgery, which would require a reapplication with data to support this use. But MSAC also noted that the descriptor for such an item would prove to be difficult to craft.

4. Background

This is the first submission for IGB for the management of moderate obesity with type 2 diabetes mellitus. MSAC has not previously considered this application.

5. Prerequisites to implementation of any funding advice

The contracted assessment (CA) identified three items that are registered for use in Australia:

- Orbera IGB is a class IIb medical device (ARTG number 226685, approved by the TGA in August 2014);
- Spatz IGB is a class IIb medical device (ARTG number 174506, approved by the TGA in August 2010); and
- Another IGB manufactured by the same applicant is an export only medical device class 1 (ARTG number 295598, approved by the TGA in October 2017).

6. Proposal for public funding

Consistent with the PICO Confirmation, the applicant proposed one item descriptor for placement of the IGB (Table 1), and another item descriptor for the removal of the IGB (Table 2).

Table 1 Proposed MBS item descriptor for IGB placement

Category 3 – Therapeutic procedures
Item no. XXXX1
Placement of IGB for a patient aged 18 years or over, with a BMI 30.0–34.9 kg/m ² who have poorly controlled T2DM (with or without other comorbidities) and who have failed first-line treatments. Can be delivered as a standalone procedure.
Multiple Services Rule (Anaes.) (Assist.) (See para T8.29 of explanatory notes to this Category)
Fee: \$redacted Benefit: Mostly 85% (with EMSN considerations), and 75% likely to be needed

Abbreviations: EMSN, extended Medicare safety net; IGB, intragastric balloon; T2DM, type 2 diabetes mellitus

Table 2 Proposed MBS item descriptor for IGB removal

Category 3 – Therapeutic procedures
Item no. XXXX2
IGB removal to which item XXXX1 applies
Multiple Services Rule (Anaes.) (Assist.) (See para T8.30 of explanatory notes to this Category)
Fee: \$redacted Benefit: Mostly 85% (with EMSN considerations), and 75% likely to be needed

Abbreviations: EMSN, extended Medicare safety net; IGB, intragastric balloon

7. Summary of Public Consultation Feedback/Consumer Issues

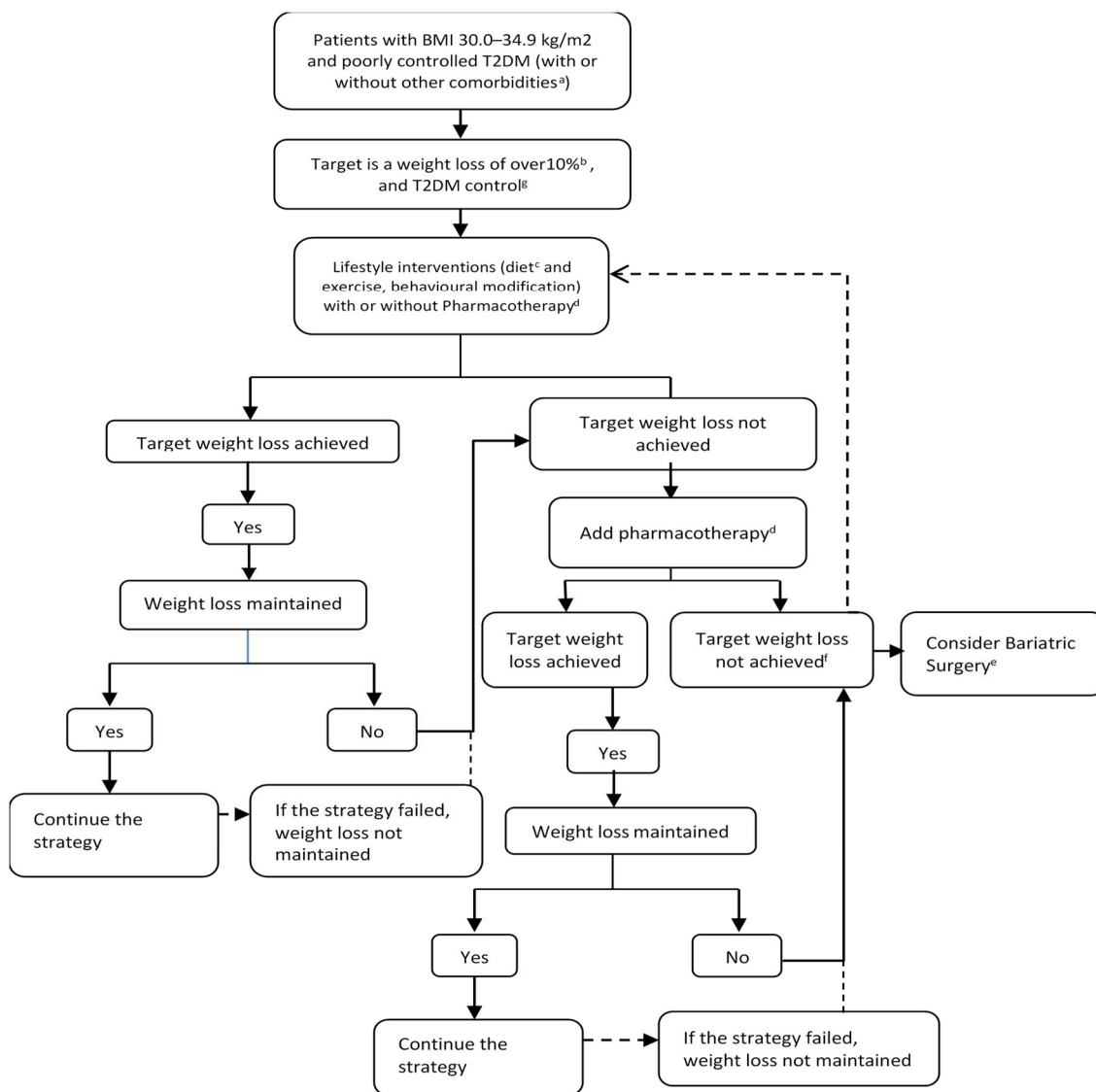
The Department received 11 responses from targeted consultations on this application, of which six were supportive and five were not. A key theme was the importance of a counselling/support program following the procedure.

8. Proposed intervention's place in clinical management

The current and proposed clinical management algorithms are presented in Figure 1 and Figure 2, respectively. The algorithm is based on the current Australian Obesity Management Algorithm developed by a working group with representatives from the Australian Diabetes Society, the Australian and New Zealand Obesity Society and Obesity Surgery Society of Australia and New Zealand. First-line treatment is lifestyle interventions (diet, exercise and behavioural modification), with or without pharmacotherapy. In patients unable to achieve target weight loss despite lifestyle intervention and pharmacotherapy, bariatric surgery may be considered. However, patients in the 30 to 34.9 kg/m² BMI group are currently not eligible for reimbursement through the MBS if they elect for bariatric surgery.

It is proposed that IGB may be an option for patients in the 30 to 34.9 kg/m² BMI group following previous failed weight loss attempts with lifestyle interventions or lifestyle and pharmacotherapy (i.e. IGB will be used in addition to lifestyle intervention).

Figure 1 Current clinical management algorithm for the treatment and management of obesity



Source: 1515 PICO Confirmation p15

Abbreviations: BMI, body mass index, T2DM, type 2 diabetes mellitus

^a Other comorbidities may include cardiovascular disease, hypertension, dyslipidaemia, kidney disease, sleep apnoea, osteoarthritis, and specific cancers.

^b As suggested by the Australian and New Zealand Obesity Society and Australian Diabetes Society (2016)

^c Diet may include reduced energy diet, low-energy diet, VLED.

^d Drugs currently registered in the TGA for the treatment of obesity are Phentermine (Duromine® and Metermine®), Orlistat (Xenical®) and Liraglutide (Saxenda®). Out of them, only Orlistat (Xenical®) is supported by PBS. Drugs options available for the management of T2DM were noted in Figure 3.

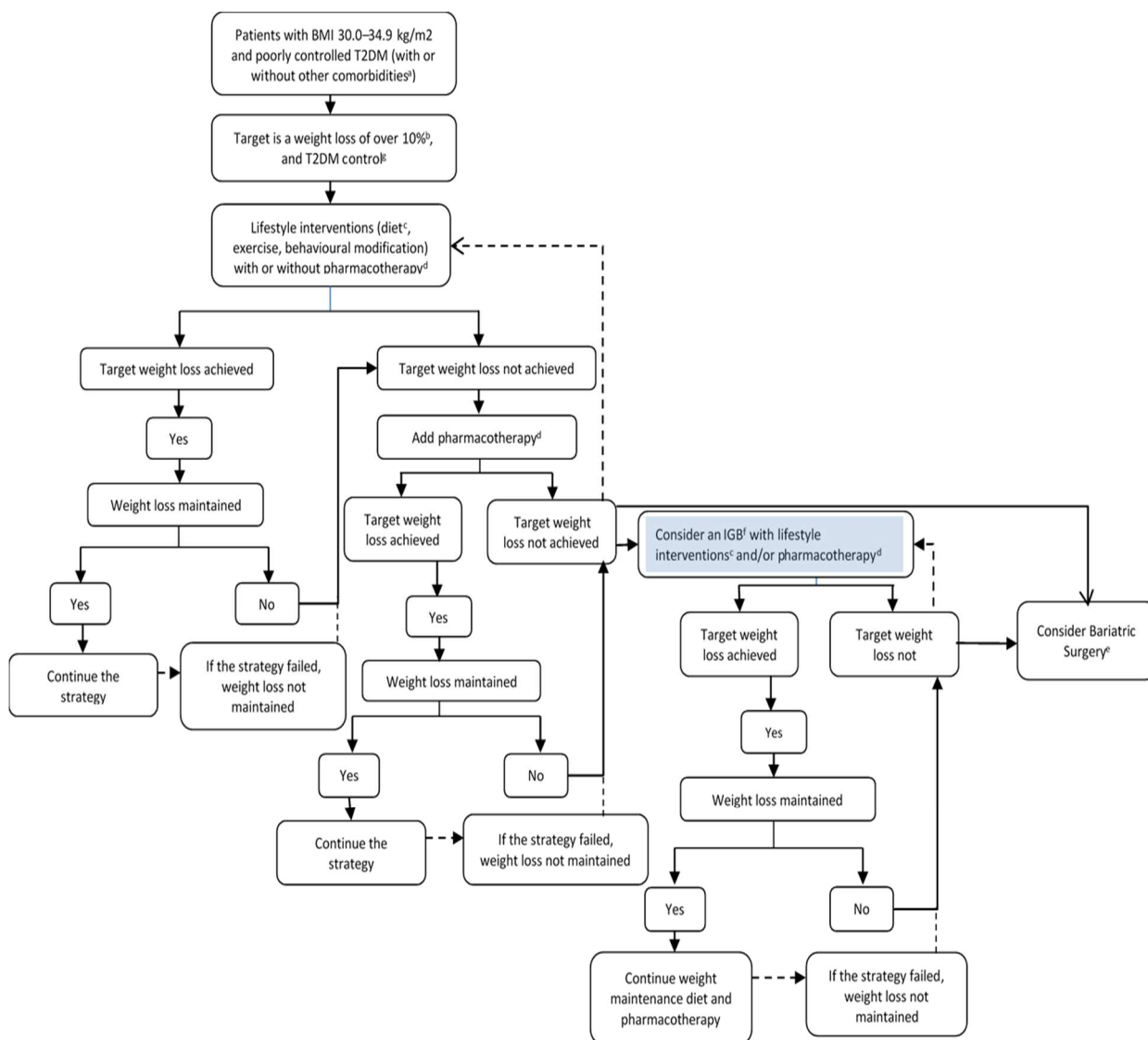
^e Australian Guidelines recommend considering bariatric surgery in the proposed IGB population. However, currently, Medicare does not reimburse for bariatric surgery in patients with BMI 30.0–34.9 Kg/m².

^f Currently most of these patients continue to cycle through diet, exercise, behavioural modifications and pharmacotherapy options or give up trying to lose weight eventually.

^g For example, diabetes remission is measured by HbA1c (<7.0%) or fasting plasma glucose level (<7mmol/L) off antidiabetic medication for a specified minimum period, and T2DM control is suggested by a reduction of ≥0.5% HbA1c in three months.

Note, Dietitians, clinical psychologists, general practitioners, physiotherapists, surgeons, gastroenterologists, endocrinologists and nurses play an essential role as a multidisciplinary team.

Figure 2 Proposed clinical management algorithm



Source: 1515 PICO Confirmation p17

^a Other comorbidities may include cardiovascular disease, hypertension, dyslipidaemia, kidney disease, sleep apnoea, osteoarthritis, and specific cancers.

^b As suggested by the Australian and New Zealand Obesity Society and Australian Diabetes Society (2016).

^c Diet may include reduced energy diet, low-energy diet, VLED.

^d Drugs currently registered in the TGA for the treatment of obesity are Phentermine (Duromine® and Metermine®), Orlistat (Xenical®) and Liraglutide (Saxenda®). Out of them, only Orlistat (Xenical®) is supported by PBS. Drugs options available for the management of T2DM were noted in Figure 1 of the PICO Confirmation.

^e Australian Guidelines recommend considering bariatric surgery for these patients. However, currently, Medicare does not reimburse for bariatric surgery in patients with BMI 30.0–34.9 Kg/m².

^f A patient may receive multiple IGBs during the lifetime. The applicant estimates that eligible patients will only have access to Orbera™ as a weight loss program at a maximum of one device per year.

^g For example, diabetes remission could be measured by HbA1c (<7%) or fasting plasma glucose level (<7mmol/L) off antidiabetic medication for a specified minimum period, and T2DM control is suggested by a reduction of ≥0.5% HbA1c in three months.

Note, Dietitians, clinical psychologists, general practitioners, physiotherapists, surgeons, gastroenterologists, endocrinologists and nurses play an essential role as a multidisciplinary team

9. Comparator

The primary comparators proposed by the PICO Confirmation are:

- lifestyle interventions (e.g. diet, exercise, behavioural modification); and

- pharmacologic interventions (including for obesity or T2DM) with lifestyle interventions.

The secondary comparator proposed by the PICO Confirmation is:

- bariatric surgery with lifestyle interventions.

The National Health and Medical Research Council (NHMRC) guidelines recommend that bariatric surgery may be considered for adults with a BMI greater than 40 kg/m² or adults with a BMI >35 kg/m² and obesity-related comorbidities. The CA stated that as the IGB is proposed for use in patients with a lower BMI than recommended for bariatric surgery, bariatric surgery is considered as a secondary comparator.

However, there was no direct evidence comparing IGB with pharmacological therapy or bariatric surgery. Therefore, lifestyle therapy is the only comparator considered in the CA's clinical evaluation.

The Critique considered the comparator might be appropriate though it does not match what was specified in the PICO confirmation. The Critique stated that the CA's narrower choice precludes assessment of IGB against bariatric surgery for those with BMI 30 to 34.9 kg/m²; the Australian and New Zealand Obesity Society and NHMRC guidelines include consideration of bariatric surgery for this patient population.

10. Comparative safety

Courcoulas 2017 (n=255; United States) and Fuller 2013 (n=74, Australia) were open-label RCTs comparing the efficacy and safety of the Orbera IGB in combination with lifestyle therapy (IGB plus lifestyle) with lifestyle therapy alone in a trial population that overlapped with the proposed MBS population (patients aged ≥ 18 years with a BMI 30 to 40 kg/m², a history of obesity for 2 years and previous failed weight loss attempts vs. patients ≥ 18 years with a BMI of 30 to 34.9 kg/m² who have poorly controlled T2DM with or without other comorbidities, and who have failed first-line treatment options).

A summary of the key safety outcomes is presented in Table 3.

Table 3 GRADE summary of findings table of key safety outcomes

Outcomes	Anticipated effects*		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Lifestyle intervention	Risk with IGB plus lifestyle intervention				
Patients who reported adverse events	708 per 1,000	984 per 1,000 (878 to 1,000)	RR 1.39 (1.24 to 1.55)	290 (1 RCT)	⊕⊖⊖⊖ VERY LOW a,b,d,e,g,h	IGB plus lifestyle intervention increases the number of people who reported adverse events, but we are uncertain.
Treatment related adverse events	Due to inconsistent reporting between studies a meta-analysis was not conducted. Both studies reported nausea, vomiting, and abdominal pain as the most common AEs experienced by the IGB group. Overall, there were significantly more treatment related AEs reported in the IGB group compared to the lifestyle group. The majority of AEs reported in the IGB group were gastric-related, whereas AEs reported in the lifestyle group were more varied in nature.			351 (2 RCTs)	⊕⊕⊕⊕ HIGH a,c,f,i,j,k	IGB plus lifestyle intervention appears to result in a large increase in treatment related adverse events compared with lifestyle intervention alone.
Device or procedure-related serious AEs	Due to inconsistent reporting between studies a meta-analysis was not conducted. For Courcoulas 2017, three procedure-related AEs occurred. Additionally, there were eight reported device-related serious AEs. Fuller 2013 did not report procedure-related AEs. Serious AEs were not predefined in Fuller 2013 study. One AE was serious enough to warrant device removal.			351 (2 RCTs)	⊕⊕⊕⊖ MODERATE a,c,f,i,j,k	IGB plus lifestyle intervention appears to result in a large increase in device or procedure-related serious AEs.

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

Abbreviations: AE, adverse events; BMI, body mass index; CI, Confidence interval; IGB, intragastric balloon; MD, Mean difference; RR, Risk ratio

GRADE Working Group grades of evidence:

⊕⊕⊕⊕ **High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect;

⊕⊕⊕⊖ **Moderate certainty:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different;

⊕⊕⊖⊖ **Low certainty:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect;

⊕⊖⊖⊖ **Very low certainty:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Studies are open label with high attrition rate. Overall high risk of bias is suspected.

b. Studies are conducted in a broader population than the PICO. Results include patients who do not have diabetes and have a BMI 35-40. It is not expected that results would be significantly different in this population. See Section C.

c. Certainty of evidence upgraded due to large magnitude of effect with no plausible confounding.

d. Single study. Body of literature is not well established, and consistency cannot be established.

e. Single study. Study conducted by sponsor. Publication bias is suspected as it is unlikely sponsor would publish negative results.

f. Results not pooled and meta-analysis unable to be conducted. Imprecision unlikely

g. No imprecision. Boundaries of the CI are on the same side of the effect threshold.

h. Significant reporting of AEs in unpublished registries. See Section B7.

i. Significant potential of reporting bias due to unblinded investigators. Can categorise AEs and their severity differently.

j. Results not pooled. Reported AEs similar between studies.

k. It is unlikely that the broader population would affect reported AEs

11. Comparative effectiveness

The Critique summarised the CA results: overall, patients in the IGB group had significantly more percentage total body weight loss, absolute weight loss and BMI reduction than the control group from baseline to 6 months and 12 months. Significantly more patients in the IGB group achieved clinically meaningful 10% total body weight loss (TBWL) compared with the control group at 6 months and 12 months. Percentage excess body weight loss (EWL) from baseline to 9 months also significantly favoured the IGB plus lifestyle over the lifestyle alone intervention. Moreover, in the IGB group, the %TBWL (at 6 months) and %EWL (at 9 months) were clinically significant in both studies. (Table 4).

However, weight regain from 6 to 12 months was substantial in both studies. The effect size of the weight loss outcomes was consistently smaller at 12 months than 6 months, with some patients gaining back more weight than lost. Given that the follow-up period is only for 12 months, it is uncertain whether the effectiveness of the IGB plus lifestyle intervention can be sustained longer term. There is a lack of RCT or high-quality observational evidence to support effectiveness beyond 12 months.

Table 4 GRADE summary of findings table of key efficacy outcomes

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Lifestyle intervention	Risk with IGB plus lifestyle intervention				
Mean percent total body weight loss from baseline follow up: mean 6 months	-	The mean percent total body weight loss from baseline in the intervention group was 7.85 % lower (10.23 lower to 5.47 lower)	-	321 (2 RCTs)	⊕○○○ VERY LOW a,b,c,d	IGB plus lifestyle intervention may reduce mean percent total body weight from baseline at 6 months but we are very uncertain.
Mean percent total body weight loss from baseline follow up: mean 12 months	-	The mean percent total body weight loss from baseline in the intervention group was 4.38 % lower (5.82 lower to 2.94 lower)	-	321 (2 RCTs)	⊕○○○ VERY LOW a,c,d,e	IGB plus lifestyle intervention may reduce mean percent total body weight from baseline at 12 months but we are very uncertain.
Percent of patients with ≥10% total body weight loss from baseline follow up: 6 months	127 per 1,000	517 per 1,000 (337 to 790)	RR 4.06 (2.65 to 6.21)	321 (2 RCTs)	⊕⊕○○ LOW a,c,d,e,f	IGB plus lifestyle intervention may increase the percent of patients with ≥10% total body weight loss from baseline at 6 months but we are very uncertain.
Percent of patients with ≥10% total body weight loss from baseline follow up: 12 months	164 per 1,000	327 per 1,000 (218 to 494)	RR 2.00 (1.33 to 3.02)	321 (2 RCTs)	⊕○○○ VERY LOW a,c,e,g	IGB plus lifestyle intervention may increase the percent of patients with ≥10% total body weight loss from baseline at 12 months but we are very uncertain.

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Lifestyle intervention	Risk with IGB plus lifestyle intervention				
Mean BMI change from baseline assessed with: Kg/m ² follow up: 6 months	-	The mean BMI change from baseline in the intervention group was 2.73 lower (3.79 lower to 1.68 lower)	-	321 (2 RCTs)	⊕⊖⊖⊖ VERY LOW a,b,c,d	IGB plus lifestyle intervention may reduce mean BMI from baseline at 6 months but we are very uncertain.
Mean BMI change from baseline assessed with: Kg/m ² follow up: 12 months	-	The mean BMI change from baseline in the intervention group was 1.26 lower (1.73 lower to 0.79 lower)	-	321 (2 RCTs)	⊕⊖⊖⊖ VERY LOW a,c,d,e	IGB plus lifestyle intervention may reduce mean BMI change from baseline at 12 months but we are very uncertain.
Absolute change of patients with diagnosis of T2DM from baseline follow up: 12 months	625 per 1,000	331 per 1,000 (112 to 969)	RR 0.53 (0.18 to 1.55)	17 (1 RCT)	⊕⊖⊖⊖ VERY LOW a,h,i,j	IGB plus lifestyle intervention may or may not reduce the number of patients with diagnosis of T2DM from baseline at 12 months.

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

Abbreviations: BMI, body mass index; CI, Confidence interval; IGB, intragastric balloon; MD, Mean difference; NR, not reported; RR, Risk ratio

GRADE Working Group grades of evidence:

⊕⊕⊕⊕ **High certainty:** We are very confident that the true effect lies close to that of the estimate of the effect;

⊕⊕⊕⊖ **Moderate certainty:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different;

⊕⊕⊖⊖ **Low certainty:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect;

⊕⊖⊖⊖ **Very low certainty:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

a. Studies are open label with high attrition rates. Overall high risk of bias is suspected.

b. Minimal overlap in confidence intervals and substantial heterogeneity (I^2 statistic).

c. Studies are conducted in a broader population than the PICO. Results include patients who do not have diabetes and have a BMI 35-40. It is not expected that results would be significantly different in this population. See Section C.

d. Small total sample size with wide CI, may affect quality of the evidence.

e. Overlap of confidence intervals and no heterogeneity ($I^2 = 0\%$).

f. Certainty of evidence upgraded due to large magnitude of effect with no plausible confounding.

g. CI of one study overlaps effect threshold.

h. Single study. Body of literature is not well established, and consistency cannot be established.

i. Patients with T2DM with a BMI 30-40. Unclear if population are between 30-35 BMI.

j. Single study. Risk difference CI overlaps effect threshold.

Clinical Claim

On the basis of the evidence profile, it is suggested that, relative to lifestyle intervention alone, IGB plus lifestyle has inferior safety and uncertain effectiveness. The Critique considered the CA's clinical claim to be reasonable.

12. Economic evaluation

A cost-utility analysis (CUA) and cost-consequence analysis (CCA) were provided, the latter due to the uncertainty in long-term clinical effectiveness of IGB plus lifestyle vs. lifestyle alone. (Table 5).

Table 5 Summary of the economic evaluation

Perspective	Australian Healthcare
Comparator	Lifestyle
Type of economic evaluation	Cost-utility (and cost-consequence)
Sources of evidence	RCTs presented in Section B (Fuller 2013 and Courcoulas 2017)
Time horizon	Lifetime (50) years in base case
Outcomes	QALYs, costs
Methods used to generate results	Markov model
Health states	BMI category (kg/m ²) < 24.9 25 to 29.9 30 to 34.9 35 to 39.9 > 40 Death
Cycle length	6 months
Discount rate	5% for costs and effects
Software packages used	Microsoft Excel

Abbreviations: BMI, body mass index; QALY, quality-adjusted life-year; RCT, randomised controlled trial

CUA

Key assumptions included:

- IGB was assumed to have a treatment benefit on T2DM calculated from rates of T2DM remission by weight loss observed in the DiRECT trial (linked evidence approach, discussed in Section C of CA); and
- BMI results from Fuller 2013 (base case) and Courcoulas 2017 (sensitivity analysis) were extrapolated to estimate impact of weight regain over time (linked evidence approach, discussed in Section C of CA).

The Critique highlighted several limitations of the CA's model:

- Disutility associated with IGB insertion, removal and adverse events were not included;
- IGB was assumed to be a one-time insertion, which was not consistent with proposed MBS descriptors;
- BMI after 2.5 years remained unchanged for the duration of the time horizon; and
- Half-cycle correction was not applied, although unlikely to have impact to lifetime horizon analysis (50 years).

The overall costs and outcomes, and incremental costs and outcomes as calculated for the intervention and comparator in the model, with the base case assumptions, are shown in Table 6.

Table 6 Incremental costs and effectiveness

	Cost	Incremental cost	Effectiveness (QALYs)	Incremental effectiveness	ICER
Step 1a Trial-based analysis (no T2DM at baseline)					
IGB plus lifestyle	\$redacted	\$redacted	-3.4	-1.5	\$redacted
Lifestyle	\$redacted		-1.9		
Step 1b Trial-based analysis (no T2DM at baseline)					
IGB plus lifestyle	\$redacted	\$redacted	1.123	0.020	\$redacted
Lifestyle	\$redacted		1.104		
Step 1c Trial-based analysis (incl.T2DM remission)					
IGB plus lifestyle	\$redacted	\$redacted	1.099	0.022	\$redacted
Lifestyle	\$redacted		1.077		
Step 2 Time horizon 5 years					
IGB plus lifestyle	\$redacted	\$redacted	3.625	0.032	\$redacted
Lifestyle	\$redacted		3.594		
Step 3 Base case - time horizon of 50 years)					
IGB plus lifestyle	\$redacted	\$redacted	12.624	0.032	\$redacted
Lifestyle	\$redacted		12.592		

Source: Edited during the critique (in italics), Table 81, pp137 of Contracted Assessment 1515

Abbreviations: ICER, Incremental Cost-Effectiveness Ratio; QALY, quality-adjusted life-year

The CA stated that the modelled results were most sensitive to the baseline BMI of patients, utility values, whether IGB was assumed to have a treatment effect on T2DM, and the duration of treatment effect of IGB on weight loss and T2DM. The Critique stated that the ICERs may accurately reflect cost-effectiveness but have a high degree of uncertainty.

CCA

The time horizon of the CCA was 12 months based on duration of pivotal RCTs. The costs and outcomes associated with T2DM were not considered in the CCA as the majority of patients in the RCTs did not have T2DM at baseline (only 7% of patients in Courcoulas 2017).

Table 7 Results of the cost-consequence analysis

	IGB plus lifestyle	Lifestyle	Difference
Costs			
Intervention costs	\$redacted	\$redacted	\$redacted
IGB device and procedure-related Serious adverse events	\$redacted	\$redacted	\$redacted
Ongoing treatment costs	\$redacted	\$redacted	\$redacted
Total	\$redacted	\$redacted	\$redacted
Outcomes (Fuller 2013)			
BMI at Month 12 (kg/m ²)	27.4	30.8	-3.4
Weight reduction from baseline (kg)	14.4	5.1	9.3
QALYs	1.123	1.104	0.020

Abbreviations: BMI, body mass index; IGB, intragastric balloon; QALY, quality-adjusted life-year

13. Financial/budgetary impacts

An epidemiological approach has been used to estimate the financial implications of the introduction of the IGB. The financial impact analysis assumes there are no other changes in the use of other medical services except those associated with the insertion and removal of the IGB. The financial implications to the MBS resulting from the proposed listing of IGB are summarised in Table 8.

Table 8 Total costs to the MBS associated with IGB insertion and removal

	2019	2020	2021	2022	2023
Estimated number of patients undertaking IGB insertion and removal	redacted	redacted	redacted	redacted	redacted
IGB insertion (proposed MBS items)					
Number of services	redacted	redacted	redacted	redacted	redacted
MBS costs	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
MBS rebate (85%)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Patient contribution	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
IGB removal (proposed MBS items)					
Number of services	redacted	redacted	redacted	redacted	redacted
MBS costs	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
MBS rebate (85%)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Patient contribution	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
IGB insertion and removal (proposed MBS items)					
Number of services	redacted	redacted	redacted	redacted	redacted
MBS costs	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
MBS rebate (85%)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Patient contribution	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
IGB insertion and removal (other MBS items)					
MBS costs	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
MBS rebate (85%)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Patient contribution	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Total cost to the MBS					
MBS costs	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
MBS rebate (85%)	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Patient contribution	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted

Abbreviations: IGB, intragastric balloon; MBS, Medical Benefits Scheme

14. Key issues from ESC for MSAC

ESC key issue	ESC advice to MSAC
Evaluation limited to 6-month Orbera IGB	Decide whether to have generic item or limit it to 6 months only.
RCT evidence covers a broader population (BMI 30–40 kg/m ²) than the application (30–34.9 kg/m ²), age limited to <65 years	Orbera safety and effectiveness is likely to be similar in the narrower BMI group. MBS bariatric surgery items have no upper age limit.
Safety concerns	Frequent adverse events and high attrition (premature IGB removal) rate are likely to reduce effectiveness.
Statistically, and probably clinically, significant short-term improvement in weight loss (vs. lifestyle) but sustainability of improvement is highly uncertain	RCT follow-up limited to 12 months. Observational studies indicate a high likelihood of substantial weight regain.
Although focus of the application is type 2 diabetes mellitus (T2DM), no high-quality evidence of T2DM control/remission is provided	While there is linked evidence from RCTs of successful weight loss, which is likely to benefit T2DM, the durability of any effect is highly uncertain. IGB has not been compared to pharmacotherapy for obesity or T2DM.
Cost of IGB	Is IGB eligible for the Prostheses List?
Item descriptor	<ul style="list-style-type: none"> • Should it be generic or specific? • Should use be limited to once per lifetime? • Should it specify that IGB is intended as an adjunct to lifestyle interventions and pharmacotherapy? • 'Failed first-line treatment' needs to be defined • Fee should be justified. • Should there be billing restrictions (e.g. co-claiming, EMSN considerations)?

ESC Discussion

Application 1515 requests Medicare Benefits Schedule (MBS) listing of the endoscopic placement and removal of an intragastric balloon (IGB) for the treatment of patients aged ≥18 years with a body mass index (BMI) of 30.0–34.9 kg/m² who have poorly controlled type 2 diabetes mellitus (T2DM) and who have failed first-line treatment options for obesity. ESC noted that this range of BMIs was chosen because these patients are not eligible for MBS rebates for bariatric surgery.

ESC noted that the title of the application has been changed to incorporate T2DM, but there is no evidence to specifically address this population.

ESC noted a number of issues with the item descriptor:

- The descriptor does not limit the number of insertions that can be performed; ESC queried whether there should be a cap on the number of services per patient. ESC noted the applicant's statement in the pre-ESC response that it is most commonly used once per lifetime, and that modelling has also been based on the assumption of once per lifetime.

- The evidence base is restricted to the Orbera device, which is currently approved by the TGA to be left in place for 6 months only. The Spatz device can be adjusted *in situ* and can be left in place for 12 months. ESC suggested that, for a generic MBS item, the descriptor could be changed to something like ‘fluid-filled, single-balloon IGB that can remain in the stomach for 6 or 12 months’.
- ‘Failed first-line treatments’ is not defined. ESC noted that the applicant clarified in their response to the PASC Outcomes that this relates to treatment for obesity, not T2DM. (MSAC may wish to consider if this is an appropriate definition). Then the descriptor should be amended to reflect this.
- The descriptor states that placement of an IGB can be delivered as a standalone procedure. However, ESC noted that it is intended to be used as an adjunct to lifestyle interventions and pharmacotherapy, which should be reflected in the descriptor.
- There is no age limit beyond 18 years; however, the evidence base is restricted to patients up to 65 years. ESC noted that MBS bariatric surgery items have no upper age limit.
- The Department commented on the applicant using a range of BMI rather than a class of obesity; however, ESC considered a BMI range to be acceptable.
- ESC noted that the same fee has been listed for both insertion and removal. Although consultation feedback suggests that device removal requires similar or higher effort compared with device placement, the applicant (in the pre-ESC response) states that both procedures take a similar amount of time and that the same fee is warranted. ESC noted that the suggested fee is **redacted** of MBS fees for endoscopic gastrointestinal procedures, which generally range from \$184 - \$357, and that this amount has not been justified.

ESC noted that the PICO specified patients with a BMI of 30–34.9 kg/m² with uncontrolled T2DM who have failed first-line treatments. However, the clinical RCT evidence is broader: patients with BMI 30–40 kg/m² who have failed first-line treatments and do not specifically have T2DM. ESC considered that Orbera safety and effectiveness is likely to be similar in the narrower BMI group.

ESC noted that PASC suggested assessment of IGB uptake rate (not from bariatric surgery) and multiple insertions; however, this has not been included in the Contracted Assessment. ESC noted that IGB plus lifestyle intervention is less safe than lifestyle intervention alone, but no comparisons were made with pharmacotherapy. ESC considered that, overall, the effectiveness of IGB plus lifestyle compared to lifestyle intervention alone is uncertain. In addition, there is a high risk of bias in both the Courcoulas (2017) and Fuller (2013) RCTs, which could be attributable to the open-label design and the attrition rate.

The meta-analysis results from the two RCTs on weight loss outcomes significantly favoured IGB plus lifestyle over lifestyle alone. However, weight regain from 6–12 months was substantial in both studies. The effect size of the weight loss outcomes was consistently smaller at 12 months than 6 months. Given that the follow-up period is only for 12 months, it is uncertain whether the effectiveness of the IGB plus lifestyle intervention can be sustained in the longer term. Specifically, there is a lack of RCT or high-quality observational evidence to support effectiveness beyond 12 months.

ESC noted that although use of an IGB resulted in more weight loss and an improved quality of life (QoL) score initially, there was substantial weight regain before the end of the follow-up period. In addition, observational studies did not support longer-term maintenance of weight loss with adjunct IGB.

ESC noted that the IGB was removed before 6 months in 9.7% of patients in the Fuller 2013 study. In Courcoulas 2017, 18.8% of patients had the device removed early due to adverse events, half of which were classified as serious adverse events of device intolerance. ESC considered that this could be a major concern, as the disutility associated with the early removal may be high, and weight loss and QoL benefits may not be achieved for these patients.

ESC noted that no probabilistic sensitivity analysis (SA) was done; only one- and two-way sensitivity analyses. The modelled results were most sensitive to baseline BMI of patients and BMI utility inputs. Specifically, changes to baseline BMI (above or below 32.5) had a large impact on the ICER. The model was also highly sensitive to the duration of treatment effect. ESC noted that the key drivers mostly favour the comparator (i.e. SA ICER > Base case ICER).

ESC noted there are several issues (as outlined by the Critique) with the estimates of budget implications, which make the financial estimates uncertain:

- The uptake rate for the IGB procedure is the most uncertain parameter and this has a large effect on estimates. PASC's suggestion to reassess uptake for IGB was partially addressed in the sensitivity analysis. Varying the bariatric surgery uptake rate by 1% each way may not sufficiently capture the high uncertainty of the parameter.
- It is unclear who bears the costs of the IGB device, which may have implications for government health budgets. ESC noted that the IGB device costs up to \$**redacted** and is not currently listed on the Prostheses List. Consequently, the IGB device cost is unlikely to be covered by private health insurance. The applicant has notified the Department that they intend to submit an application for the device to be prostheses listed, pending the MSAC outcome.
- Costs of complications, adverse events and monthly visits to an operating physician were not included in the estimation of budget implications, so the budget impact is underestimated.

ESC confirmed that this is a Type C procedure: it is usually done as a day-hospital procedure.

15. Other significant factors

Nil

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

Apollo is committed to making Orbera available to patients who are not eligible for bariatric surgery. Orbera provides an effective treatment option for some people with moderate obesity (Class I obesity: body mass index (BMI) 30-34.9 kg/m²) with T2DM; these patients having tried and failed first line treatment options including lifestyle modification and pharmacotherapy (both of which have demonstrated very limited effectiveness in providing sustainable weight reduction). Of all the endoscopic bariatric therapies, IGBs, and specifically Orbera, have the greatest amount of clinical experience with over 350 clinical publications globally including randomised evidence supporting their use (American Society for Gastrointestinal Endoscopy 2015, Stavrou, Tsaousi et al. 2019). IGB placement has been established as a relatively straightforward, safe and well tolerated, minimally invasive procedure for obesity management, by filling the gap between numerous conventional measures and bariatric surgery (Laing, Pham et al. 2017). All the adverse events that occurred globally up to date have been self-reported by Apollo Endosurgery and we will continue

doing this, as we are conscious about the safety of our products. The American Society for Gastrointestinal Endoscopy (ASGE) systematic review and meta-analysis of endoscopic bariatric therapies reports that pain and nausea are the most common side effect of Orbera with serious AEs rare (an incidence of migration and gastric perforation of 1.4% and 0.1%, respectively). Orbera is the most widely reported on balloon in peer review literature. Any patient death related to a medical procedure is a tragedy. Orbera has a strong safety profile with gastric perforation rate of 0.01%, Esophageal perforation <0.01%, Pancreatitis of <0.01% and spontaneous hyperinflation of 0.07% with a global mortality rate of less than 0.01% (or, less than 1% of 1%), and more than 295,000 Orbera balloons have been distributed worldwide. Further evidence of the value of Orbera is the addition of IGBs to the American Society for Metabolic and Bariatric Surgery (ASMBS) list of approved procedures and devices in 2018 following IGB approvals by the FDA in 2015 (Aminian, Chang et al. 2018). Lastly with regards to long term data, Apollo did provide data on patients 3 years post removal (Genco et al. 2013) which shows that patients average BMI is reduced after 3 years, with many patients maintaining the weight loss achieved by the 6-month balloon treatment in the medium term (42 months) (Genco, Lopez-Nava et al. 2013). Mean BMI fell from 28.6 ± 0.4 at baseline to 25.4 ± 2.6 kg/m² at 6 months and to 27.0 ± 3.1 kg/m² at 3 years from Orbera removal. The mean % excess weight loss (EWL) was 55.6 % at 6 months and 29.1 % at 3 years. At 3 years the incidence of diabetes as a co-morbidity was still reduced from baseline (i.e. 15% of patients at baseline, 8% at 6 months and 10% at 3 years). The demonstrated ongoing benefit in reducing co-morbidities is clinically important, with co-morbidities the main driver of obesity-related health expenditure in Class 1 obesity in Australia (Buchmueller and Johar 2015). There is a need for less-invasive weight loss interventions to bridge the current gap in our management approach to obesity and also to improve access to treatment options.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: [visit the MSAC website](#)