Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1612 – Prostatic urethral lift procedure for men with benign prostate hyperplasia

Applicant: **Teleflex Australia Pty Ltd**

Date of MSAC consideration: **MSAC 79th Meeting, 28-29 July 2020**

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 a fee increase for an existing Medicare Benefits Schedule (MBS) item 36811 for the prostatic urethral lift (PUL) procedure for men with benign prostate hyperplasia (BPH) was received from Teleflex Australia Pty Ltd 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 deferred its advice on the request for an increase in the MBS fee for PUL procedure for BPH. MSAC considered that PUL is likely inferior in terms of effectiveness to transurethral resection of the prostate (TURP) and visual laser ablation of the prostate (VLAP). MSAC considered PUL has a different safety profile to TURP, and that the comparative safety of PUL versus VLAP is unclear. MSAC noted there are significant uncertainties in the costs associated with each procedure, and requested a further holistic assessment of the different therapeutic approaches to BPH management that takes into account the different outcomes and costs associated with each. MSAC recognised that individual patients may have different preferences when considering the balance between side effects and long-term effectiveness.

Consumer summary
Teleflex Australia Pty Ltd requested a fee increase for the prostatic urethral lift (PUL) procedure to treat benign prostate hyperplasia (BPH). PUL is currently on the Medicare Benefits Schedule (MBS) under a generic item for non-specific procedures. BPH is a non-cancerous enlargement of a person's prostate that occurs as a natural part of ageing. This can cause lower urinary tract symptoms, such as increased frequency, urgency and/or difficulty in urinating, which can impact the person's quality of life. In a PUL procedure, a doctor (usually an urologist) inserts a device into the urethra (where urine

Consumer summary

comes out). When the device reaches the side of the prostate, it ejects small, thin implants into both sides of the prostate, helping to open the urine channel. This relieves some of the symptoms of an enlarged prostate, such as problems urinating.

MSAC noted that there are other MBS funded procedures for treating BPH and that BPH is commonly treated using transurethral resection of the prostate (TURP), which involves the surgical removal of prostatic tissues through the urethra. MSAC noted that PUL was safe, and had some better outcomes (such as maintaining ejaculatory function) compared to other MBS funded procedures used to treat BPH. However, PUL does not seem to work as well as other procedures in the long term. This means that many patients may have short-term relief after a PUL procedure, but their symptoms may come back and the person will need to have either another PUL or a different procedure.

MSAC acknowledged the importance of patient preference and options, and that some patients may value the benefits of PUL.

MSAC's advice to the Commonwealth Minister for Health

MSAC decided to defer its advice regarding the fee increase for PUL. MSAC would like to review all the procedures used to treat prostate enlargement, and compare their advantages and disadvantages with regards to their effectiveness, safety, cost and cost-effectiveness. This will help MSAC estimate the appropriate fees for each procedure. MSAC recognised that individual patients may have different preferences when considering the balance between side effects and long-term effectiveness. In the meantime, PUL is still available on the MBS for those who wish to have it.

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

MSAC noted that this application requested a fee increase for an existing MBS item 36811 for the PUL procedure for men with BPH.

MSAC recalled that the TURP (MBS item 37203) fee is $1,058.80 and, in March 2019, MSAC supported an increase in VLAP (MBS item 37207) fee from $866.45 to match TURP on the basis of non-inferiority. The proposal in this submission was to increase the fee for PUL to $1,058.80.

PUL is currently funded under MBS item 36811 CYSTOSCOPY with insertion of urethral prosthesis (with the fee of $328.55). This is a generic item and used also for other non-specific procedures. MSAC noted the applicant's suggestion that this fee discrepancy is a disincentive to perform PUL on the basis of inequality in fees for procedures of equal efficacy. However, MSAC noted that utilisation of VLAP did not increase after its fee increase.

MSAC noted that the comparative clinical evidence was based on three randomised clinical trials: BPH6 (PUL *vs.* TURP), L.I.F.T. (PUL *vs.* sham) and GOLIATH (VLAP *vs.* TURP). MSAC noted that the composite endpoint used to claim superiority of PUL *vs.* TURP in the BPH6 study was comprised of six outcomes, with safety and erectile/ejaculatory outcomes driving the BPH6 endpoint. This biased the study against TURP. In addition, the 22% withdraw rate in the BPH6 study was not addressed.

Regarding safety, MSAC noted that retrograde ejaculation is the most common long-term complication of TURP (in up to 90% of cases). However, MSAC noted that retrograde ejaculation is not considered to be a serious long-term complication. Some degree of urinary incontinence and erectile dysfunction are also common after TURP. MSAC considered it reasonable to conclude PUL has superior safety compared with TURP in terms of function and procedure but MSAC noted that prostheses-related adverse events for PUL are unknown. There were no studies comparing safety of PUL and VLAP; thus, MSAC considered the safety profile of PUL compared with VLAP to be unknown.

Regarding effectiveness, MSAC noted the clinical claim for PUL is non-inferior effectiveness compared to TURP, based on the BPH6 composite endpoint. After 1 year, PUL is non-inferior to TURP for the BPH6 endpoint. After 2 years, PUL appears to be inferior to TURP for IPSS and urinary flow scores, but PUL is superior to TURP for ejaculatory function scores. MSAC noted the reintervention rates at 2 years for PUL (13.6%) and TURP (5.7%) where patients go on to require VLAP, TURP, repeat PUL or Botox® for detrusor overactivity. MSAC thus acknowledged that, for patients who wanted to preserve ejaculatory function, PUL may be preferable to TURP, but considered PUL to have inferior effectiveness compared to TURP overall. MSAC noted that the GOLIATH trial showed that VLAP has non-inferior effectiveness to TURP, making it likely that PUL has inferior effectiveness compared to VLAP.

MSAC noted that the economic evaluation was a cost-comparison analysis, but MSAC queried whether a cost-effectiveness analysis or cost-utility analysis may be more appropriate, given that the clinical claim of non-inferiority was not well supported. MSAC noted that the Department revisited the cost comparison calculations following ESC advice, which showed that at the proposed fee of $1,058.80 PUL could be more costly than TURP and VLAP, which is inconsistent with a finding of inferiority.

MSAC further noted that the cost of PUL may be underestimated due to the costs and number of implants required and the re-intervention rate not being adequately accounted for, and that the cost of TURP and VLAP may be overestimated, including major complications, length of stay and capital costs.

MSAC noted the uncertainty regarding the financial impact due to the number of PUL procedures being displaced, rather than substituted.

MSAC considered that the treatments for BPH management required a more holistic review, and recommended that the Department, in consultation with applicants and professional and consumer stakeholders, undertake a review of the effectiveness (including short and long-term outcomes), safety, costs and cost-effectiveness of VLAP, PUL, TUWA, TUNA, TURP and any other procedures used to manage BPH.

MSAC considered this review could also usefully garner information on:

- why urologists recommended certain procedures
- what informs patient preferences for certain procedures
- long-term outcomes.

This review will allow MSAC to provide better advice to the Minister on which BPH procedures should be funded on the MBS and the appropriate fees for each procedure.

4. Background

This is the first submission requesting a fee increase for an existing MBS item 36811 for prostatic urethral lift procedure for men with benign prostate hyperplasia, which was first listed on the MBS on 1 May 1997.

5. Prerequisites to implementation of any funding advice

Items on the Australian Register of Therapeutic Goods (ARTG) that are relevant to this application are shown in Table 1. The UroLift® prosthesis, implanted as part of the procedure, is also listed on the Prostheses List.

Table 1 UroLift® System listed on the ARTG

ARTG no.	Product no.	Product description	Product category	Sponsor
200361	58882	Prostatic retraction implant	Medical Device Class IIb	Teleflex Medical Australia Pty Ltd

Abbreviations: ARTG = Australian Register of Therapeutic Goods.
Source: Therapeutic Goods Administration, accessed 8th January 2020 Link to TGA.gov.au

6. Proposal for public funding

Prostatic urethral lift is currently funded for the treatment of men with benign prostate hyperplasia (BPH) on the MBS under Item 36811 CYSTOSCOPY with insertion of urethral prosthesis (with the fee of $328.55).

The MBS item descriptor with increased fee proposed by the applicant is summarised in Table 2.

Table 2 Proposed MBS Item 36811 Descriptor

Category 3 – Therapeutic Procedures
CYSTOSCOPY with insertion of urethral prostheses
Multiple Operation Rule
(Anaes.)
Fee: $1,058.80 Benefit: 75% = $794.10

Source: Table 1, p13 of the Applicant Developed Assessment Report (ADAR).

The commentary noted that this item is currently used for both males and females, and was in existence prior to the introduction of the UroLift system. If MSAC decides to support a fee increase for PUL, there may be a need to create a separate item specific for patients with BPH.

7. Summary of public consultation feedback/consumer Issues

Public consultation responses was received from two organisations, the Urological Society of Australia and New Zealand (USANZ; healthcare specialists) and Private Healthcare Australia (PHA; representative body for Private Health Insurance Industry). A patient testimonial in support of PUL was also provided as part of the pre-MSAC response.

The response from the USANZ noted the benefits of PUL, including the minimally invasive nature of the procedure and associated improvements in surgical duration, blood loss, hospital length of stay and preservation of sexual function. Overall, the USANZ were supportive of the application. However, it was noted that: 1) longer term outcomes in terms of sustained clinical improvement and safety remains largely unknown, and 2) there is a size limit for the prostate gland, and this procedure does not change the actual prostate size.

The response from the PHA was not supportive of the application. The PHA noted that PUL is a minimally invasive and short procedure and therefore the fee for PUL should not be equivalent to the fee for TURP, a more complex surgical procedure. The PHA stated that an average of 3.1 fixation devices are currently used per patient on the Prostheses List and claimed that increasing the MBS fee for PUL would make PUL the most expensive urological implant on the Prostheses List (and one of the 30 most expensive billing codes on the entire list).

8. Proposed intervention's place in clinical management

Description of Proposed Intervention

The PUL procedure is conducted by installing small permanent implants transurethrally under endoscopic guidance to lift apart the obstructing lateral lobes and reduce urethral obstruction. The procedural objective is to create a channel through the anterior aspect of the prostatic fossa. The implant is comprised of a monofilament with a nitinol capsular tab on one end and a stainless steel urethral end-piece on the other.

After rigid cystoscopy, the implant delivery device (UroLift System), which houses a 2.9 mm telescope, is inserted into a 20F sheath and angled laterally (20-30 degrees) usually at the 10 and 2 o'clock position to compress the anterior third of the obstructive lobe. The delivery device laterally deploys a 19 gauge needle through the lobe. As the needle is withdrawn, the capsular tab of the implant engages the prostatic capsule. The monofilament is then tensioned, cut to the specific width of the compressed lobe, and secured in place by the urethral end-piece. Thus, each implant is customized in length and location in situ based on an individual's prostate anatomy. Because the fibromuscular capsule is less compliant than the periurethral tissue, the capsular tab holds firmly in place while the urethral end-piece holds the lobe apart to expand the urethral lumen. The narrow urethral end-piece invaginates into the urethral wall where epithelialization occurs.

Description of Medical Condition

BPH, also called prostate enlargement, is a non-cancerous enlargement of the prostate gland, in which smooth muscle and epithelial cells proliferate, which occurs as a natural part of ageing. Symptoms may include frequent urination, trouble starting to urinate, weak stream, inability to urinate, or loss of bladder control. It is estimated 2.4 million Australian men over the aged of 50 suffer from an enlarged prostate or BPH. More than 50% of men over the age of 60 are diagnosed with BPH and by 85 the number climbs to 90%.

Patients proposed to be eligible for the proposed medical service would have the following:

- Age > 50 years
- Prostate volume <100mL
- International Prostate Symptom Score (IPSS) > 12.

The clinical management algorithm and the proposed place of PUL is presented in Figure 1.

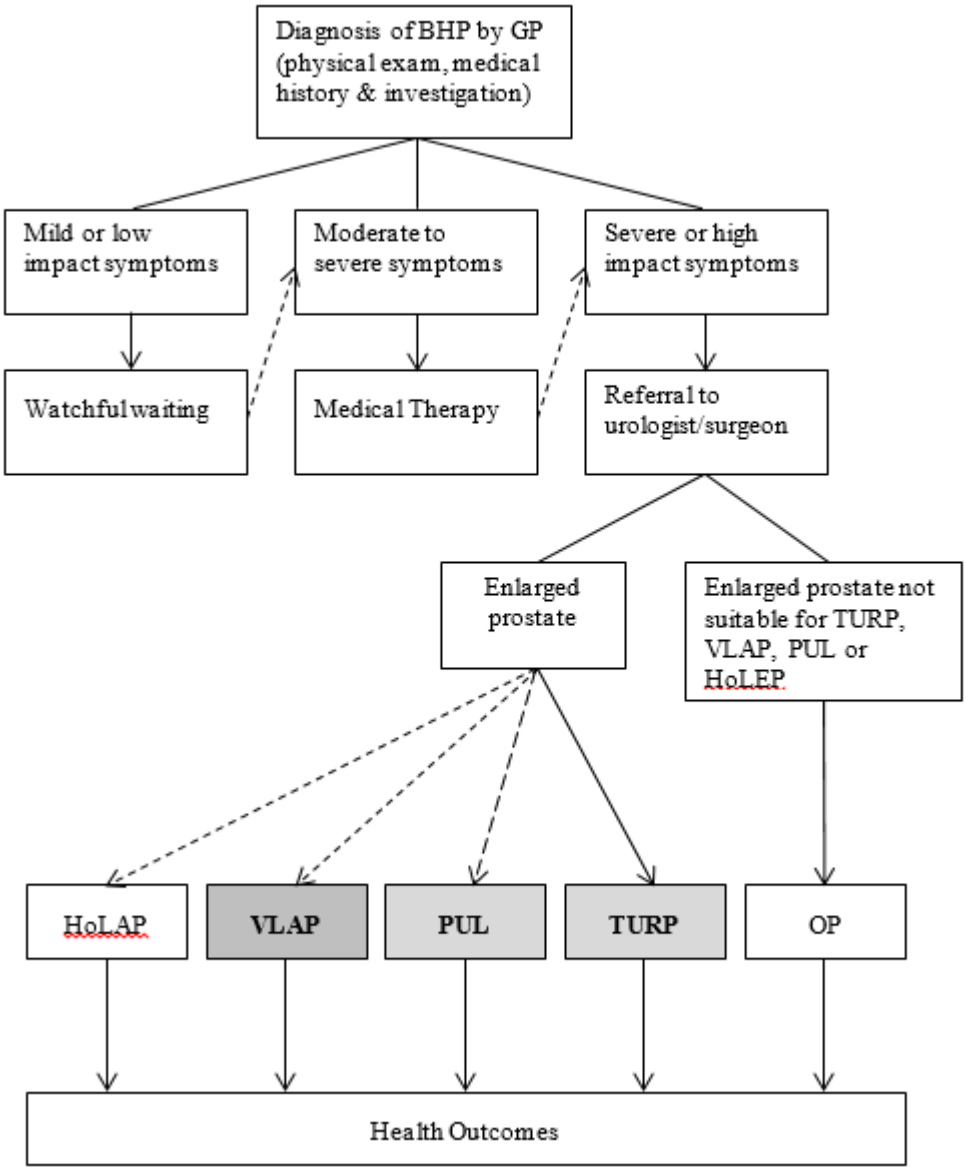

Figure 1 Clinical management algorithm for PUL relative to TURP or VLAP

Abbreviations: HoLEP = Holmium laser enucleation of the prostate; LUTS = lower urinary tract symptoms; OP = open prostatectomy; PUL = prostatic urethral lift; TUMT = transurethral microwave thermotherapy; TURP = transurethral resection of the prostate; TUWA = transurethral water ablation; VLAP = visual laser ablation of the prostate.
Source: Figure 1, p28 of the ADAR.

The commentary noted that the ADAR had used the clinical management algorithm from MSAC assessment 1518 even though this was inconsistent with the proposed indications for use of PUL. The clinical management algorithm suggests that only patients with severe or high impact symptoms of BPH would be referred to a urologist for PUL, TURP, or visual laser ablation of the prostate (VLAP), whereas the indications for PUL suggest that patients with moderate to severe symptoms (based on a score of >12 on the IPSS) would be eligible.

The commentary presented an alternative clinical algorithm (Figure 2) adapted from the Canadian Urological Association guidelines (adapted to remove techniques not listed on the MBS) (Nickel et al. 2018[1]). This is the same clinical algorithm in the European guidelines, which has been endorsed by the Urological Society of Australia and New Zealand. In this algorithm the options recommended differ depending on prostate size and ability to tolerate

[1] Nickel JC, Aaron L, Barkin J, Elterman D, Nachabe M & Zorn KC (2018). Can Urol Assoc J 12(10): 303-312.

anaesthesia and stop antiplatelet and anticoagulants. The treatment listed first in each box is the current standard/first choice in Canada for the respective subgroup. In the subpopulation of men who cannot tolerate anaesthesia, transurethral microwave thermotherapy (TUMT) or transurethral water vapour ablation (TUWA) may be more appropriate comparators than TURP.

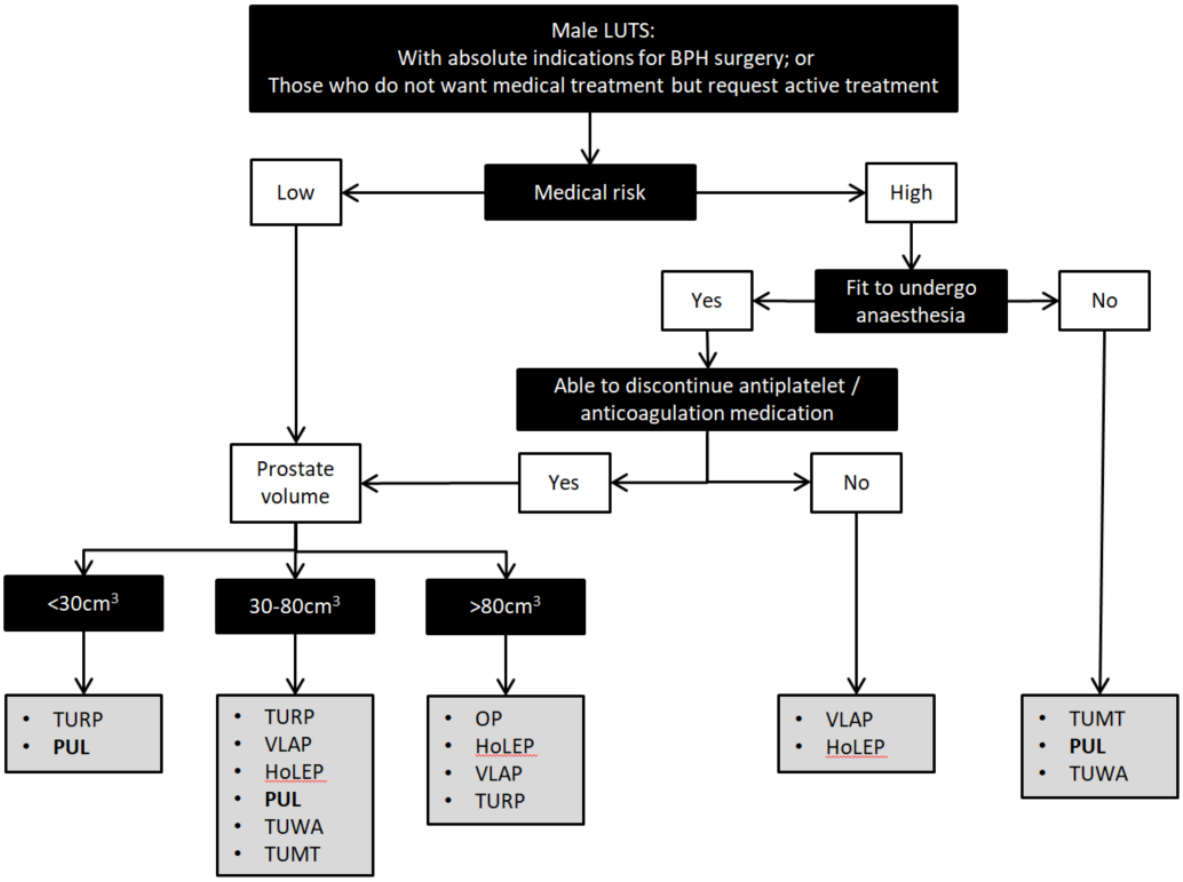

Figure 2: Clinical management algorithm adapted from Canadian Urological Association guideline on male lower urinary tract symptoms/benign prostatic hyperplasia (MLUTS/BPH): 2018

Abbreviations: HoLEP = Holmium laser enucleation of the prostate; LUTS = lower urinary tract symptoms; OP = open prostatectomy; PUL = prostatic urethral lift; TUMT = transurethral microwave thermotherapy; TURP = transurethral resection of the prostate; TUWA = transurethral water ablation; VLAP = visual laser ablation of the prostate.
Source: Figure 2, p45 of the commentary.

9. Comparator

TURP

The applicant proposed the main comparator to PUL is TURP. TURP is considered the gold standard procedure by many authors for BPH patients when a reduction of prostate tissue is necessary (Teo, Lee & Ho 2017[2]). In Australia, the practise of TURP is not restricted to prostates of any particular size. There are two forms – monopolar (M-TURP) and bipolar (B-TURP).

In the monopolar procedure, a high frequency current from a generator is passed through an active electrode, enabling electro-resection via a resectoscope. Lighting and irrigation enable vision for the surgeon while resecting the vascular organ. Pieces of tissue separated from the prostate are flushed into the bladder and then from the body. Bleeding is a common event

[2] Teo JS, Lee YM & Ho HSS (2017). Asian Journal of Urology 4(3): 6-15.

occurring with incidence of bleeding requiring transfusion of 0.4%-7.1% (Teo, Lee & Ho 2017).

Bipolar TURP, although less frequently practised in Australia, was introduced as an alternative to help reduce side effects of M-TURP. It induces tissue disintegration through molecular dissociation with a high frequency energy. One advantage of the technique is that is can be used with saline irrigation. Placement of active and return electrodes mean high current densities are local and thermal damage to surrounding tissue is reduced. Although trial outcomes have been mixed, it is possible that blood loss is likely to be smaller with B-TURP compared to M-TURP (EAU 2016[3]; Teo, Lee & Ho 2017).

TURP syndrome is a serious complication which can occur with TURP. It is thought to be caused by the use of irrigation fluids of lower osmolality than serum during the procedure. Perforation of capsular veins and sinuses may occur as a result. TURP syndrome is characterised by mental confusion, nausea, vomiting, hypertension and bradycardia, and can lead to cerebral oedema and sometimes death. Preventative measures should be taken to avoid this side effect.

TURP can provide a sample of prostatic tissue for histology analysis, which occasionally identifies tumour cells.

The commentary considered TURP an appropriate main comparator for patients who are fit enough to undergo a general or spinal anaesthesia, and able to discontinue antiplatelet or anticoagulation medications.

The MBS item descriptor for TURP is shown in Table 3.

Table 3 Relevant MBS item for the comparator, TURP

Category 3 – Therapeutic Procedures
MBS Item 37203 PROSTATECTOMY (endoscopic, using diathermy or cold punch), with or without cystoscopy and with or without urethroscopy, and including services to which item 36854, 37201, 37202, 37207, 37208, 37245, 37303, 37321 or 37324 applies Multiple Operation Rule (Anaes.) Fee: $1,058.80 Benefit: 75% = $794.10

Source: Table 14, p27 of the ADAR.

VLAP

The MSAC Executive specifically requested that this application include VLAP as an alternative comparator. An application for a fee increase to the same level as TURP for VLAP was recently recommended by MSAC (Application 1518).

VLAP, also called photoselective vaporisation of the prostate (PVP), can be performed using a number of laser systems which have the capability of being focused and selectively coagulating or vaporising prostate tissue. The laser systems use a side-firing technique and can be used with an endoscope through the urethra. Ablation of the prostate by VLAP is practised in Australia on enlarged prostates of any size.

VLAP is not a treatment for prostate cancer, and if a malignancy is suspected, a biopsy of the prostate is conducted as a separate procedure to VLAP.

[3] EAU (2016). "Treatment of non-neurogenic male LUTS." European Association of Urology Guidelines.

The MBS item descriptor for VLAP is shown in Table 4.

Table 4 Relevant MBS item for the alternative comparator, VLAP

Category 3 – Therapeutic Procedures
MBS Item 37207 PROSTATE, endoscopic non-contact (side firing) visual laser ablation, with or without cystoscopy and with or without urethroscopy, and including services to which items 36854, 37201, 37202, 37203, 37206, 37245, 37321 or 37324 applies *Multiple services rule* (Anaes.) Fee: $1,058.80 Benefit: 75% = $794.10

Source: Table 15, p27 of the ADAR.

Additional comparators

The commentary noted that in patients who cannot tolerate general or spinal anaesthesia, transurethral microwave thermotherapy (TUMT; MBS item 37230, fee $1,058.80) or TUWA (for which MBS claims are currently being accepted under MBS item 37201 for transurethral radio-frequency needle ablation (TUNA), fee $842.10) may be used. The clinical management algorithm shown in Figure 2 in section 6 shows that these would be appropriate comparators to PUL for this subpopulation. TUNA is also listed for use in patients who are not medically fit for TURP (MBS item 37201, fee $842.10). For the broader population of patients with BPH, the TUMT and TUNA procedures are not considered best practice in Australia, and are rarely used (PICO confirmation for MSAC application 1518).

Other minimally invasive techniques for treating BPH exist, but have not been able to use pre-existing MBS items. Given the lack of MBS items, it may be appropriate that they weren't considered comparators for this application.

10. Comparative safety

The ADAR included 13 citations that reported on two comparative clinical trials (BPH6[4] and L.I.F.T[5] studies) and four non-comparative studies relevant to PUL. The BPH6 study directly compared PUL to the main comparator, TURP, while the L.I.F.T study compared PUL to a sham procedure.

No clinical trials or case studies were identified in the ADAR literature search that directly compared PUL to VLAP. However, the ADAR included the GOLIATH[6] study for the clinical comparison between VLAP and TURP.

The commentary noted that despite 13 citations being listed as 'included', only the results of a single trial (from two articles) were provided on the comparison of PUL and TURP. The justification for restricting the evidence to randomised trials was not provided. No information was provided on how PUL compares against other minimally invasive techniques in patients not eligible for TURP (those who cannot tolerate anaesthesia or stop anticoagulants or antiplatelet medication).

[4] Comparison of the UroLift System to TURP for Benign Prostatic Hyperplasia (BPH-6) - NCT01533038; cited in Sønksen et al. 2015 and Gratzke et al. 2017.

[5] Luminal Improvement Following Prostatic Tissue Approximation for the Treatment of LUTS secondary to BPH; cited in Roehrborn et al. 2013; McVary et al. 2014; Cantwell et al. 2014; Roehrborn et al. 2015; Rukstalis et al. 2016; McVary et al. 2017; Rukstalis et al. 2019

[6] A Prospective Multicenter Randomized Study Comparing Photoselective Vaporization of the Prostate With the GreenLight XPS™ Laser System and Transurethral Resection of the Prostate for the Treatment of Benign Prostatic Hyperplasia; cited in Bachman et al. 2014.

The commentary also noted that the GOLIATH study was not retrieved as part of the ADAR literature search. It is unclear how this paper was retrieved.

The pre-ESC response clarified that the BPH6 study (two citations) is the only study that directly compared PUL to TURP. The other eleven studies were mainly used to support the economic/financial evaluation. The applicant also provided the abstract of Patel et al (2019)[7] which reviewed the Manufacturer and User Facility Device Experience Database. The applicant stated that this paper concluded that 'each BPH modality investigated (TURP, PUL, HoLEP, VLAP) had minimal patient harm with over 99% of patients experiencing no complication after device malfunction'.

PUL versus TURP

The main evidence for the comparison of safety between PUL (n=45) and TURP (n=35) came from the BPH6 study which was reported at 12 and 24 months (shown in Table 5). Although the BPH6 study was randomised, ten patients randomised to the TURP arm declined treatment. This study was not blinded and the outcome measure was a composite endpoint made up of:

- LUTS relief – reduction of ≥ 30% in IPSS at 12 months compared to baseline
- Recovery experience – QoR VAS ≥ 70 by 1 month
- Erectile function – reduction of ≤ 6 points for SHIM during 12 months follow-up
- Ejaculation function – response to MSHQ-EjD
- Continence preservation – ISI score of ≤4 points at all follow-up intervals
- Safety – no treatment adverse events > grade 1 on the Clavien-Dindo classification system at any time during the procedure or follow-up.

In order to meet responder status, it was required that patients experienced no treatment-related adverse event greater than grade I on the Clavien-Dindo classification system at any time during the procedure or follow up. In the BHP6 study a threshold of grade II+ was selected to account for events that might significantly affect a patient's postoperative course, such as those requiring surgery, endoscopy, radiology, or supranormal pharmacology. If a patient pursues secondary treatment, the failure to respond is captured in the effectiveness element (#1) and not the safety element (#6); the patient is therefore censored from the safety element analysis at all subsequent time points.

The commentary noted that the Clavien-Dindo classification system was developed to assess surgical complications, rather than prostheses-related adverse events. This may therefore bias the safety results in favour of PUL (as prostheses-related adverse events are relevant to PUL but not TURP).

The commentary noted that the safety of the procedures can be stratified as relating to function (e.g. ejaculation), surgery (e.g. post-operative complications), and prosthesis-related (e.g. device fragmentation). The BPH6 study only reported on the first two types of safety outcomes. Rates of most types of adverse events were non-significantly different between PUL and TURP, however, urinary incontinence and retrograde ejaculation were significantly more common in patients who underwent TURP than PUL. However, it is unknown how frequently prosthesis-related adverse events occur after PUL (this type of adverse event is not applicable to TURP).

[7] Patel NH, Uppaluri N, Iorga M, Schulman A, Bloom JB, Phillips J, Fullerton S, Konno S, Choudhury M & Eshghi M (2019) Journal of endourology 33(6): 448-454.

Table 5 Key features of the included evidence (BPH6 study) comparing PUL with TURP

Author	Sønksen et al	Gratzke et al
PMID	25937539	27862831
Pub Year	2015	2017
Study Design	Prospective, randomized, multinational, controlled, non-blinded study (BPH6)	Prospective, randomized, multinational, controlled, non-blinded study (BPH6)
Location	Denmark, UK, Italy, Germany No centres in Italy were included, only Denmark, UK and Germany	Denmark, UK, Italy, Germany No centres in Italy were included, only Denmark, UK and Germany
Follow-up	12 months	24 months
Study Population	Men ≥aged 50 yr, IPSS > 12, Prostate volume ≤ 60 cm3, Qmax 15 ml/s for 125-ml voided volume, sexually active within 6 months before the index procedure, SHIM score > 6, ISI score ≤ 4, positive response to MSHQ-EjD (excluding the response "could not ejaculate")	Men ≥aged 50 yr, IPSS > 12, Prostate volume ≤ 60 cm3, Qmax 15 ml/s for 125-ml voided volume, sexually active within 6 months before the index procedure, SHIM score > 6, ISI score ≤ 4, positive response to MSHQ-EjD (excluding the response "could not ejaculate")
Exclusion criteria	Active urinary tract infection at time of treatment, bacterial prostatitis within 1yr of the index procedure, cystolithiasis within 3mo of the index procedure, obstructive median lobe, current urinary retention, urethral condition that may prevent insertion of a rigid 20F cystoscope, previous TURP or laser procedure, pelvic surgery or irradiation, prostate-specific antigen ≥10ng/L, history of prostate or bladder cancer, severe cardiac comorbidities, anticoagulants within 3d of the index procedure, other medical condition or co-morbidity contraindicative for TURP or PUL, unwilling to report sexual function. Declined treatment	
Population size	80 men	80 men
Intervention	Prostatic urethral lift	Prostatic urethral lift
Comparator	TURP	TURP
Outcomes	The BPH6 responder endpoint assesses symptom relief, quality of recovery, erectile function preservation, ejaculatory function preservation, continence preservation, and safety. Preservation of ejaculation and quality of recovery were superior with PUL ($p<0.01$). Significant symptom relief was achieved in both treatment arms. The study demonstrated not only non-inferiority but also superiority of PUL over TURP on the BPH6 endpoint.	Change in IPSS and Qmax in the TURP arm were superior to the PUL arm. Improvements in IPSS QoL and BPHII score were not statistically different between the study arms. PUL resulted in superior quality of recovery, ejaculatory function preservation and performance on the composite BPH6 index. Ejaculatory function bother scores did not change significantly in either treatment arm. Only PUL resulted in statistically significant improvement in sleep.
Reintervention	Reintervention for failure to cure occurred in 6.8% (3/44) of PUL and 5.7% (2/35) of TURP patients (not significant).	At 2 years PUL had 13.6% retreatment. TURP had 5.7%.

Abbreviations: IPSS = International Prostate Symptom Score; SHIM = Sexual Health Inventory for Men; ISI = Incontinence Severity Score; MSHC-EjD = Male Sexual Health Questionnaire for Ejaculatory Dysfunction; TURP = transurethral resection of the prostate; PUL = prostatic urethral lift.
Source: Table 17, p57 of the commentary.

VLAP versus TURP

No clinical trials or case studies were identified by the ADAR that directly compared the intervention PUL to the additional comparator VLAP.

As such the safety of PUL compared to VLAP is unknown.

However, the ADAR included the GOLIATH study for the clinical comparison between VLAP and TURP. The GOLIATH study (N=281) was a prospective, randomized, non-blinded controlled trial with a 24 month follow up. The primary outcome was the IPSS for which a margin of three was used to evaluate the non-inferiority of VLAP to TURP.

Secondary outcomes included Qmax, prostate volume, prostate specific antigen, Overactive Bladder Questionnaire Short Form, International Consultation on Incontinence Questionnaire Short Form, occurrence of surgical retreatment and freedom from complications.

11. Comparative effectiveness

PUL versus TURP

The comparative clinical effectiveness of PUL versus TURP is based on the two year results of the BHP6 trial that used the composite BPH6 index as the endpoint. The summary of findings from the BPH6 study is shown in Table 6. The proportion of patients who met the BPH6 primary endpoint was found to favour PUL vs TURP (non-inferiority P = 0.0002, superiority P = 0.006).

On the basis of the benefits and harms reported in the evidence base (summarised below), the ADAR suggested that, relative to TURP, PUL has non-inferior safety and effectiveness.

Table 6 Balance of clinical benefits and harms of PUL, relative to TURP, and as measured by the critical patient-relevant outcomes in the key study – BPH6 at 24 months

Endpoint		PUL (SD)	TURP (SD)	Difference	
IPSS Score	Baseline	21.4 (5.5)	22.8 (5.9)		
	24 months change	-9.2 (9.2)* significant improvement	-15.3 (7.5)* significant improvement	P value 0.004	Significant favours TURP
Qmax (ml/s)	Baseline	9.3 (3.4)	9.6 (3.4)		
	24 months change	14.3 (5.3)* significant improvement	25.5 (17.2)* significant improvement	P value 0.002	Significant favours TURP
PVR (ml)	Baseline	80.5 (61.0)	98.8 (87.1)		
	24 months change	-10.6 (56.7)	-42.5 (91.7)* significant improvement	P value 0.091	Not significant
IPSS-QoL	Baseline	4.6 (1.1)	4.6 (1.2)		
	24 months	2.1 (1.6)* significant improvement	1.3 (1.5)* significant improvement	P value 0.066	Not significant
SHIM	Baseline	20.4 (4.5)	18.5 (5.3)		
	24 months Change	-0.2 (4.3)	-1.8 (4.9)	P value 0.201	Not significant
MSHQ-EjD	Baseline	10.6 (2.8)	8.9 (2.3)		
	24 months	10.9 (3.3)	4.9 (4.6)* significant deterioration	P value 0.001	Significant favours PUL

Abbreviations: IPSS = International Prostate Symptoms Score (decreased score indicates symptom relief), IPSS-QoL = International Prostate Symptoms Score – Quality of Life (decreased score indicates improvement); PVR = post-void residual urine volume (decreased score indicates better quality of recovery), SHIM, sexual health inventory for men (decreased score suggests improvement). *Hochberg method for multiple testing corrected P value >0.05 for difference between baseline and 24 months. MSHQ-EjD - Ejaculatory Dysfunction (increased score suggests improvement), Qmax = peak flow rate (increase suggests better quality of recovery).
Source: Table 2, p18 of the commentary

The commentary noted that, in order to be defined as a responder in the BHP6 study, all of the thresholds had to be met. An unweighted composite measure which combines five safety outcomes and only one effectiveness outcome is biased against TURP.

The commentary noted that the key measure of LUTS relief, the IPSS score, showed that TURP was significantly better than PUL at reducing symptoms. The average patient who underwent PUL still had moderate severity BPH at 24 months (mean IPSS = 12.2), which remained above the minimum IPSS required to be eligible for PUL (IPSS >12).

The commentary considered that based on the results of the BPH6, a more appropriate clinical claim for PUL would be superior safety and inferior effectiveness to TURP in patients with moderate to severe BPH. For patients in whom ejaculatory functioning is a key priority, PUL may be the preferred option, despite not being as effective at reducing symptoms of BPH as TURP. However, the commentary considered the two procedures cannot be claimed to be equivalent.

VLAP versus TURP

On the basis of the benefits and harms reported in the evidence base (summarised in Table 7 below), the ADAR suggested that, relative to TURP, VLAP has non-inferior safety and effectiveness.

Table 7 Balance of clinical benefits and harms of VLAP, relative to TURP, and as measured by the critical patient-relevant outcomes in the GOLIATH study at 24 months

Endpoint		VLAP	TURP	Difference	
IPSS Score	Baseline	21.2 ± 5.9	21.7 ± 6.4		
	24 months	6.9 ± 6.0	5.9 ± 6.1	1.0 [-0.5, 2.5]	Non-inferior
Qmax (ml/s)	Baseline	9.5 ± 3.0	9.9 ± 3.5		
	24 months	21.6 ± 10.7	22.9 ± 9.3	-1.3 [-4.0, 1.4]	Non-inferior
PVR (ml)	Baseline	110.1 ± 88.5	109.8 ± 103.9		
Suggest no	24 months	45.6 ± 65.5	34.9 ± 47.1	P value 0.2	Not significant
IPSS-QoL	Baseline	4.6 ± 1.1	4.5 ± 1.4		
	24 months	1.3 ± 1.2	1.2 ± 1.3	P value 0.6	Not significant
IIEF-5	Baseline	13.2 ± 7.6	13.7 ± 7.5		
	24 months	12.9 + 7.5	13.9 + 8.2	P value 0.3	Not significant

Abbreviations: IIEF-5 = International Index of Erectile Function-5; IPSS = International Prostate Symptoms Score; IPSS-QoL = International Prostate Symptoms Score – Quality of Life; PVR = post-void residual urine volume; Qmax = peak flow rate.
Source: Table 3, p19 of the commentary

The commentary considered that given the non-inferiority of TURP and VLAP, and that PUL is inferior to TURP on the IPSS and Qmax, it is suggested that PUL would have inferior effectiveness to VLAP. The safety of PUL compared to VLAP is unknown.

No information was provided on how PUL compares against other minimally invasive techniques in patients not eligible for TURP (those who cannot tolerate anaesthesia or stop anticoagulants or antiplatelet medication).

Clinical claim

On the basis of the evidence provided, the applicant claimed that relative to TURP:

- PUL has non-inferior safety and effectiveness.
- VLAP has non-inferior safety and effectiveness.

12. Economic evaluation

The ADAR presented a cost-comparison comparing PUL with the comparators TURP and VLAP (Table 8).

Table 8 Summary of the economic evaluation

Perspective	MBS and Private Health Insurers
Comparator	TURP or VLAP
Type of economic evaluation	Cost comparison
Sources of evidence	Systematic review
Time horizon	Two or five years
Outcomes	Cost per procedure
Methods used to generate results	Bottom up costing of procedures
Discount rate	5%
Software packages used	ExCel

Source: Table 4, p21 of the commentary.

The commentary noted that as the claim of non-inferiority is not well supported, the cost-comparison approach presented may not be appropriate.

The key assumptions in the application included:

- MBS item numbers: Since PUL, VLAP and TURP are currently MBS listed, the use of the current item numbers for the surgeon and the anaesthetist was considered justified. Note that the fee used for VLAP is that recommended as a result of MSAC Application 1518, that is, the same as TURP.
- AR-DRG data cube 2017-18: Most recent available.
- 2019 Private Hospital Fee Schedule for Workers Compensation Theatre Banding and bed-day fee: Although considered to be a very conservative estimate, this fee schedule covers 2019 private hospitals.
- IHPA National Efficient Price Determination 2018-19: This provided up to date relative cost weight between TURP with major complications and TURP with minor complications.
- Prostheses List February 2020: Most up to date benefit amount for the UroLift prosthesis.
- Sievert et al (2019): Real world study as opposed to a controlled clinical study. Believed to more accurately reflect actual usage. Also confirmed by Eure et al (2019) paper.
- Hospital length of stay (LoS): significant difference between PUL and TURP.
- TURP – major/minor complications: significant difference in cost between major and minor.
- Prostheses: Cost of PUL sensitive to number implanted.
- VLAP capital and disposable costs sourced from a Queensland paper by Whitty et al (2014) and capital cost updated using CPI increase 2013 to 2019.

The pre-ESC response clarified that the time horizon of five years was used as this was the maximum follow-up published from clinical studies and was appropriate for the economic analysis.

The overall costs, as calculated by the applicant for the intervention (PUL) and comparators (TURP and VLAP), are shown below in Table 9 – 10, 11 – 13 and 15.

TURP

The procedure costs for TURP (shown in Table 23, p52 of the ADAR) used a combination of current MBS Fees for the surgeon and the Anaesthetist, 2019 Private Hospital Fee Schedule

for Workers Compensation Theatre Banding and bed-day fee, to derive a total cost per procedure of $4,971.8 (based on the bed-days for minor complications).

The commentary noted that the length of hospital stay with TURP, 2.56 days, was based on the average length of hospital stay for AR-DRG L05B[8] in the AIHW National Hospital Morbidity Database (2017-18). The ADAR has not justified using a longer hospital stay for TURP than what was observed in the BPH6 study (2.56 v 1.9 days), while assuming the length of stay observed in BPH6 for PUL (1 day).

The pre-MSAC response clarified that the hospital stays used for the costing of the procedures, 2.56 days for TURP and overnight for PUL, were based on Australian practice rather than the international stays in the BPH6 study. The pre-MSAC response acknowledged that the cost of the disposable loops were omitted in the ADAR's costing of TURP (Table 9) and therefore, the pre-MSAC response provided updated costing of TURP that includes the TURP disposable loops (see Table 9) which derived a total cost per TURP procedure of $5454.06.

Table 9 TURP Procedure Cost (updated in pre-MSAC response)

Medicare payments -75% scheduled fee	MBS Item	Fee	Health Fund	Medicare
Pre-anaesthesia consultation	17610	$44.35	$11.05	$33.30
Initiation of management of anaesthesia 7 units	20914	$140.70	$35.15	$105.55
Anaesthesia – time (46-60 minutes)	23045	$80.40	$20.10	$60.30
Procedure – surgeon	37203	$1,058.80	$264.70	$794.10
Theatre - minor complications – Band 5		$1,501.50	$1,501.50	$0.00
Bed-days @ $838.30 /day for 2.56 days		$2,146.05	$2,146.05	$0.00
TURP disposable loop		$482.26	$482.26	$0.00
Addition cost to the PBS		??		
Total		$5,454.06	$4,460.81	$993.25

Source: Table 23, p3 of the pre-MSAC response.

The ADAR stated the AR-DRG data cube 2017-18 divides TURP by major and minor complications.

Table 10 TURP – major and minor complications

	Separations	Patient Days	Av.
L05A Transurethral Prostatectomy for Urinary Disorder, Major Complexity	656	5309	8.09
L05B Transurethral Prostatectomy for Urinary Disorder, Minor Complexity	4795	12256	2.56
Total	5451	17565	3.22

Source: Table 6, p18 of the ADAR.

According to the IHPA National Efficient Price Determination 2018-19, the cost weight for L05A was 3.1643 and 1.3024 for L05B. Using these cost weights and the minor complications procedure cost for TURP calculated in Table 23, p52 of the ADAR, the ADAR calculated the procedure cost for TURP major complications s $12,079.44. Thus, the average TURP procedure cost, calculated as 12% of procedures with complications at $12,079.44 and 88% of procedures without complications at $4,971.80, is $5,824.72.

[8] Transurethral Prostatectomy for Urinary Disorder, Minor Complexity

The commentary noted that as described above, the inclusion of major complications costs for TURP only, and not for PUL (or VLAP) has not been justified. Further, the cost weight and split of major to minor complications used may not be reasonable.

The pre-MSAC response provided updated calculations based on the updated TURP procedure costs shown above in Table 9 and the cost weights for L05A and L05B shown in Table 10. Using these cost weights and the minor complications procedure cost of $5,454.06 for TURP, the procedure cost for TURP major complications is $13,251.14. Thus, the average TURP procedure cost, based on 12% of procedures being with major complications and 88% with minor complications, is $6,389.71. The applicant noted that this is $121.52 higher than the $6,268.19 adjusted cost for PUL (Table 11 below). The applicant claimed inclusion of the cost of TURP procedures with major complications results in a financial saving to both the MBS and the Private Health Funds for each patient 'swapped' to PUL.

PUL

Table 11 PUL Procedure Cost (updated in pre-MSAC response)

	MBS Item	Fee	Health Fund	Medicare
Pre-anaesthesia consultation	17610	$44.35	$11.05	$33.30
Initiation of management of anaesthesia	20902	$80.40	$20.10	$60.30
Anaesthesia – time (46-60 minutes)	23045	$80.40	$20.10	$60.30
Procedure – surgeon	36811	$1,058.80	$264.70	$794.10
Theatre – Band 2		$617.30	$617.30	$0.00
Bed-days - one day (overnight)		$789.10	$789.10	$0.00
Prostheses 4 @ $712 each		$2,848.00	$2,848.00	$0.00
Capital (5 years / 50 patients / 5%)		$148.90	$148.90	$0.00
Annual maintenance per patient		$24.00	$24.00	$0.00
Reintervention @ 1.44% of TURP cost		$78.54	$64.24	$14.30
Additional prosthesis 0.7 @ $712		$498.4	$498.4	$0.00
Total		$6,268.19	$5,305.89	$962.30

[a] The MBS item quoted is for anorectal procedures. If the number of units is considered reasonable, then it may be more appropriate to use MBS item 20910, which is *also for* transurethral procedures (noting that the same fee applies to both).
Source: Table 26, p3 of the pre-MSAC response.

Table 12 Capital calculations

Cystoscopy camera/ monitor set	$25,000.00
Irrigation system	$5,000.00
Standard endoscopic grasper set kit	$2,000.00
Total capital	$32,000
Annual cost (discounted @ 5%)	$7,445.00
Annual cost per patient (50 patients)	$148.90
Annual maintenance contract	$1,200.00
Annual maintenance per patient	$24.00

Source: p23 of the commentary.

The commentary noted that the total cost of PUL, including reintervention, is estimated in the ADAR to be $5,775.13. The main component of PUL cost is that of the prostheses. As the ADAR may have underestimated the average number of prostheses implanted, did not consider a prostheses handling fee and likely underestimated both the proportion of patients

expected to require reintervention and the cost of reintervention, the cost of PUL is likely to be an underestimate, and the cost savings claimed, likely to be further overestimated.

The pre-ESC response clarified that the number of prostheses implanted depends on the size of the subject's prostate and that the ADAR estimated the number of prostheses used was four based on data from Sievert et al (2019). The applicant acknowledged that the sensitivity analysis carried out as part of the ADAR identified that the costing model is sensitive to the number of prostheses implanted. However, the applicant claimed the commentary's estimate of 3.1 prostheses based on feedback from Private Healthcare Australia to be a low estimate that does not align with number in published papers.

The pre-ESC response also clarified that:

- the net annual reintervention rate used in the model was 1.44% for each of the five years and that this annual cost was added to the total cost of PUL
- there is no handling fee, and
- the cost of the prosthesis, $712, was taken from the Prostheses List.

VLAP

Table 13 VLAP Procedure Cost

	MBS Item	Fee	Health Fund	Medicare
Pre-anaesthesia consultation	17610	$44.35	$11.05	$33.30
Initiation of management of anaesthesia	20902 [a]	$80.40	$20.10	$60.30
Anaesthesia – time (61-75 minutes)	23055	$100.50	$25.10	$75.40
Procedure – surgeon	37207	$1,058.80	$264.70	$794.10
Theatre – Band 2		$617.30	$617.30	$0.00
Bed-days - two days		$1,578.20	$1,578.20	$0.00
Capital (5 years / 50 patients / 5%)		$913.19	$913.19	$0.00
Annual service cost (50 patients)		$358.00	$358.00	$0.00
Fibre cost per patient (mean)		$1,242.00	$1,242.00	$0.00
Total		$5,992.74	$5,029.64	$963.10

[a] The MBS item quoted is for anorectal procedures. If the number of units is considered reasonable, then it may be more appropriate to use MBS item 20910, which is also *for transurethral procedures (noting that the same fee applies to both).*
Source: Table 8, p24 of the commentary.

Table 14 Capital calculations

Laser machine	$166,000.00
Four cystoscopes and adapter	$9,994.00
Alterations to theatres	$1,000.00
Total capital (2013 values)	$176,994.00
Total capital (2019 values)*	$196,251.00
Annual cost (discounted @ 5%)	$45,659.28
Annual cost per patient (50 patients)	$913.19
Annual maintenance contract	$1,7900.00
Annual maintenance per patient	$358.00

* CPI increase 2013 to 2019 = 10.88%
Source: p25 of the commentary.

PUL relative to TURP and VLAP

Table 15 Disaggregated and aggregated incremental cost of PUL relative to TURP and VLAP

	PUL	TURP	Incremental cost of PUL	VLAP	Incremental cost of PUL
Procedure cost without complications					
• Procedure costs	$1,058.80 [a]	$1,058.80	$0.00	$1,058.80	$0.00
• Anaesthesia costs	$205.15	$265.45	–$60.30	$225.25	–$20.10
• Hospital (non-procedure) costs	$1,406.40	$3,647.55	–$2,241.15	$2,195.50	–$789.10
• Prostheses/consumables costs	$2,848.00	$0.00	$2,848.00	$1,242.00	$1,606.00
• Capital and maintenance costs	$172.90	$0.00	$172.90	$1,271.19	–$1,098.28
• Reintervention costs	$83.88	$0.00	$83.88	$0.00	$83.88
Subtotal	**$5,775.13**	**$4,971.80**	**$803.33**	**$5,992.74**	**–$217.61**
Proportion with complications	-	12%		-	
Procedure cost with complications	-	$12,079.44		-	
Total	**$5,775.13**	**$5,824.72**	**–$49.59**	**$5,992.74**	**–$217.61**

[a] Proposed PUL MBS fee.
Abbreviations: PUL = prosthetic urethral lift; TURP = transurethral resection of the prostate; VLAP = visual laser ablation of the prostate.
Source: ADAR Critique Table 1, p25 of the commentary.

The commentary noted that relative to TURP, the ADAR estimates that PUL is associated with a slight cost saving ($49.59). This is due to costs related to major complications with TURP being included in the analysis, which may not be reasonable. Relative to VLAP, the ADAR estimates that PUL is associated with a cost saving of $217.61. This is driven by cost offsets related to a reduction in hospital costs and capital expenditure. The assumption of differential hospital costs (due to a longer assumed length of stay) has not been justified. Further, the assumptions used to estimate the per patient capital costs (50 patients per year over 5 years) may not be reasonable.

The commentary considered that the cost of PUL is likely to be underestimated, given the assumptions regarding the number of prostheses and reintervention. Therefore, the cost savings claimed, is likely to be overestimated.

The modelled results were most sensitive to the number of prostheses (PUL), number of bed-days (TURP) and life of capital (VLAP) as shown in Table 16.

Table 16 Key drivers of the economic model

Description	Method/Value	Impact
PUL - Number of prostheses	Increase from 4 to 4.5 (12.5%)	+ $356.00
TURP – Number of bed-days	Increase from 3.22 to 3.62 (12.5%)	+ $337.42
TURP – Number of bed-days	*Increase from 2.56 to 2.88 (12.5% increase)*	*−$309.75*
VLAP – Life of capital	Increase from 5 to 7 years	-$228.38

Note: Analyses in italics were conducted by the commentary as the results presented in the ADAR could not be verified.
Abbreviations: PUL = prosthetic urethral lift; TURP = transurethral resection of the prostate; VLAP = visual laser ablation of the prostate.
Source: Table 9, p26 of the commentary.

The commentary noted that the sensitivity analyses presented in the ADAR were based on arbitrary increases (12.5% for the number of PUL prostheses or number of TURP bed days, or 2 year increase for VLAP capital). These arbitrary values do not reflect the range of uncertainty in the parameters tested. Additional sensitivity analyses conducted by the commentary are presented in Table 17.

Table 17 Sensitivity analyses conducted by the commentary

	PUL	TURP	Inc. cost	VLAP	Inc. cost
Base case	**$5,775.13**	**$5,824.72**	**–$49.59**	**$5,992.74**	**–$217.61**
Hospital length of stay					
*TURP, 1.9 days (base case: 2.56) **(#5)***	*$5,765.79*	*$5,176.52*	*$589.27*	*$5,992.74*	*–$226.94*
VLAP, 1 day (base case: 2 days)	*$5,775.13*	*$5,824.72*	*–$49.59*	*$5,203.64*	*$571.49*
Source of TURP major cost weight multiplier (base case: 2018-19, 2.43)					
*2019-20 (2.13) **(#1)***	*$5,772.58*	*$5,647.82*	*$124.76*	*$5,992.74*	*–$220.16*
2020-21 (1.98)	*$5,771.30*	*$5,559.16*	*$212.14*	*$5,992.74*	*–$221.43*
Proportion of TURP major complications, 6%[a] (base case: 12%)	*$5,768.99*	*$5,398.26*	*$370.73*	*$5,992.74*	*–$223.75*
No. PUL prostheses implanted (base case: 4)					
*4.7 **(#6)***	*$6,273.53*	*$5,824.72*	*$448.81*	*$5,992.74*	*$280.79*
3.1 [b]	*$5,134.33*	*$5,824.72*	*-$690.39*	*$5,992.74*	*-$858.41*
Prosthesis handling fee (5%) included (base case: not included)	*$5,917.53*	*$5,824.72*	*$92.81*	*$5,992.74*	*–$75.21*
No. VLAP fibres, 1.08 (base case: 1.38)	*$5,775.13*	*$5,824.72*	*–$49.59*	*$5,722.74*	*$52.39*
*VLAP capital cost, $254.15 [c] (base case: $913.19) **(#3)***	*$5,775.13*	*$5,824.72*	*–$49.59*	*$5,333.70*	*$441.42*
*VLAP capital maintenance costs, $179 [d] (base case: $358) **(#3)***	*$5,775.13*	*$5,824.72*	*–$49.59*	*$5,813.74*	*–$38.61*
Reintervention cost after PUL, $6.105.77 (base case: $5,824.72)	*$5,779.17*	*$5,824.72*	*–$45.54*	*$5,992.74*	*–$213.56*
Proportion of additional reintervention after PUL (base case: 1.44%)					
*7.2% **(#2)***	*$6,110.63*	*$5,824.72*	*$285.92*	*$5,992.74*	*$117.89*
7.9%	*$6,151.40*	*$5,824.72*	*$326.69*	*$5,992.74*	*$158.67*
*Inclusion of TURP disposable loop costs [e] (base case: not included) **(#4)***	*$5,782.07*	*$6,306.98*	*–$524.91*	*$5,992.74*	*–$210.66*
PHDB AR-DRG hospital cost data [f] (2.56 days of TURP, 2 day of VLAP)	*$5,661.00*	*$5,763.67*	*−$102.67*	*$7,265.53*	*−$1,604.54*
PHDB AR-DRG hospital cost data [f] (1.9 days of TURP, 1 day of VLAP)	*$5,644.52*	*$4,619.13*	*$1,025.38*	*$5,531.38*	*$113.13*
Multivariate analyses					
#1 AND #2	*$6,097.89*	*$5,647.82*	*$450.07*	*$5,992.74*	*$105.16*
#1, #2 AND #3	*$6,097.89*	*$5,647.82*	*$450.07*	*$5,154.70*	*$943.19*
#1, #2, #3 AND #4	*$6,131.56*	*$6,115.44*	*$16.12*	*$5,154.70*	*$976.86*
#1, #2, #3, #4 AND #5	*$6,086.31*	*$5,486.93*	*$599.38*	*$5,154.70*	*$931.61*
#1, #2, #3, #4, #5 AND #6	*$6,584.71*	*$5,486.93*	*$1,097.78*	*$5,154.70*	*$1,430.01*

Abbreviations: PHDB = Private Hospital Data Bureau; PUL = prosthetic urethral lift; TURP = transurethral resection of the prostate; VLAP = visual laser ablation of the prostate.

[a] Proportion of Clavien-Dindo grade 3b bleeding events with TURP in the BPH6 study. Note that this was not significantly different to the proportion of Clavien-Dindo grade 3b bleeding events with PUL in the BPH6 study.

[b] The average number of prostheses implanted per patient as reported in the Private Healthcare Australia targeted consultation feedback. It should be noted however that this number is lower than the average number of prostheses used in the BPH6 trial that was the basis for the claim of non-inferiority. The ADAR did not consider whether the number of implants used would affect the relative treatment effect if PUL.

[c] Assuming the VLAP capital costs are amortised over 10 years, assuming 100 patients per year (base case: discounted over 5 years, assuming 50 patients per year).

[d] Assuming 100 patients per year (base case: 50 patients per year).

[e] 1.1278 loops, as per the GOLIATH trial, at a cost of $365 each assumed, based on Whitty et al. (2014).

f The average hospital cost per day was estimated from the average cost of TURP separation presented in ADAR Critique Table 15 ($1,734). This was applied per day stay for TURP and VLAP. No additional costs were applied to account for TURP complexity as the AR-DRG costs already consider this. The average cost of PUL hospitalisation was applied as estimated in ADAR Critique Table 15 ($1,293).

Source: ADAR Commentary Table 3, p26 of the commentary

The multivariate analyses conducted by the commentary provide alternate assumptions in a stepped manner (i.e. TURP cost weight multiplier, using the five-year reintervention rate rather than the annualised rate applied once, VLAP capital assumptions, TURP consumables and length of hospital stay and number of PUL prostheses). The commentary proposed that MSAC may wish to consider whether the base case should be respecified to apply these

changes. PUL was observed to be associated with substantial costs when these alternate assumptions were changed at the same time.

The commentary considers the proposed increase in fee not well justified given that the claim of non-inferiority was not well supported in the ADAR, and that PUL may be associated with substantial additional costs.

In the pre-ESC response, the applicant noted the commentary's analysis used a bed-day stay of 1.9 days for TURP. According to the IHPA National Efficient Price Determination 2018-19 the length of stay for TURP with minor complications, ignoring the impact of including with major complications, was 2.56 days. The multivariate analysis also (incorrectly) looked at the effect of a 5% handling fee.

Table 18 ESC Revised multivariate sensitivity analysis: Disaggregated and aggregated incremental cost of PUL relative to TURP and VLAP (revised inputs in italic text)

	PUL	TURP	Incremental cost of PUL	VLAP	Incremental cost of PUL
Procedure cost without complications					
• Procedure costs	$ 1,058.80	$ 1,058.80	$ -	$ 1,058.80	$ -
• Anaesthesia costs	$ 205.15	$ 265.45	-$ 60.30	$ 225.25	-$ 20.10
• Hospital (non-procedure) costs	$ 1,406.40	$ 3,647.55	-$ 2,241.15	*$ 1,406.40*[e]	$ -
• Prostheses/consumables costs	*$ 3,346.40*[a]	*$ 412.45*[c]	$2,933.95	$ 1,242.00	$ 2,104.40
• Capital and maintenance costs	$ 172.90	$ -	$ 172.90	*$ 433.15*[f]	-$ 60.25
• Reintervention costs	*$ 445.65*[b]	$ -	$ 445.65	$ -	$ 445.65
Subtotal	**$ 6,635.30**	**$5,384.25**	**$1,251.05**	**$ 4,365.60**	**$ 2,269.70**
Proportion with complications	-	*6%*[d]		-	
Procedure cost with complications	-	*$ 10,589.9*[d]		-	
Total	$ 6,635.30	$6,019.65	**$615.65**	$ 4,365.60	**$ 2,269.70**

a = 4.7 prostheses per procedure
b = 7.2% overall re-intervention rate (at higher number of prosthesis)
c = 1.13 loops at $365 per loop
d = cost weight multiplier 2.13 (versus 2.43); proportion major complications 6% (versus 12%)
e = no difference in hospital costs for VLAP versus PUL
f = VLAP capital and maintenance costs revised per commentary ($433.15 vs $1271.19)

The pre-MSAC response reiterated that:

- The ADAR included a net annual reintervention rate of 1.44% for each of the five years post PUL and was added to the total cost of PUL when comparing procedure costs.
- The sensitivity analysis determined the modelled results were most sensitive to the number of prostheses used and re-justified the assumption that an average of 4 devices is used in each PUL procedure.
- The cost of TURP is most sensitive to the length and cost of stay, and re-justified the use of 2.56 days at a cost of $838.30 in the ADAR based on the IHPA National Efficient Price Determination 2018-19 in which the length of stay for TURP with minor complications, ignoring the impact of including with major complications, was 2.56 days.
- The hospital stays used for the costing of the procedures, 2.56 days for TURP and overnight for PUL, were based on Australian practice rather than the international stays in the BPH6 study.

13. Financial/budgetary impacts

The financial implications to the MBS resulting from the proposed increased fee for PUL, summarised by the ADAR with modifications by the commentary, are presented in Table 19.

The current fee for PUL (MBS Item 36811) is $328.55 of which the MBS pays $246.45 (75%). The proposed fee is $1,058.80 (the same as TURP) of which the MBS would pay $794.10 (75%). Thus, the incremental cost to the MBS is $547.65.

The ADAR estimate assumed an annual 10% growth in PUL with the additional patients swapping from TURP. It also assumes that both procedures, PUL and TURP, are performed as inpatient procedures. Since the proposed fee is the same as TURP, any increase in the use of PUL resulting from a switch from TURP has a zero incremental impact.

The commentary clarified that the ADAR assumed that with the proposed fee increase for PUL, estimated utilisation would be comprised of (#1) those services that would have occurred in the absence of the fee change; and (#2) a proportion of services that switch from TURP to PUL due to the fee change. As a comparison, data presented at ESC showed that the VLAP price increase was not related to increased utilisation. Table 18 includes modifications by the commentary to distinguish between these services.

Table 18 Additional costs to the MBS associated with increase fee for PUL

PUL	2020-21	2021-22	2022-23	2023-24	2024-25
Existing PUL services (#1)	1,230	1,230	1,230	1,230	1,230
Incremental cost to the MBS per service	$547.65				
Cost to the MBS	$673,610	$673,610	$673,610	$673,610	$673,610
Existing TURP services that switch (#2)	–	123	258	407	571
Incremental cost to the MBS per service	$0.00				
Cost to the MBS	$0.00	$0.00	$0.00	$0.00	$0.00
Number of services	1,230	1,353	1,488	1,637	1,800 1,801
Total	$673,610	$673,610	$673,610	$673,610	$673,610

Source: Table 10, p28 of the commentary.

The commentary noted that in estimating #1, the ADAR assumed that the number of services would remain the same over the projected period (i.e. 1,230 service per year), and so does not consider an increase in services due to population growth (which may not be reasonable). Furthermore, the approach taken does not take into account the generic nature of MBS item 36811. This item is not specific to PUL and is used for cystoscopy with insertion of any urethral prostheses. Given the three-fold proposed fee increase, use of this item in other indications may substantially increase.

While the number of PUL services that would have occurred in the absence of the fee change was not estimated to change over the projected period, the total number of PUL services was estimated to increase by 10% per year. No justification was provided for this estimate. This was comprised totally of services that would have switched from TURP to PUL (i.e. #2, Table 18). However, the ADAR has not considered that some of these reduced TURP services would be displaced rather than replaced by PUL, due to reintervention. While the net difference in the rate of reintervention was considered in the cost-comparison analysis, this was not included in the estimates of financial impact.

The 75% MBS Benefit is proposed to increase from $246.45 to $794.10 (i.e. $547.65 increase). In estimating the increase in cost to the MBS due to the proposed increase in the fee for MBS item 36811, the ADAR applied the difference in the 75% MBS Benefit (i.e. $547.65) to those patients who would have received PUL irrespective of the fee change (i.e. #1 in Table 19). As the proposed MBS fee is the same as the current fee for TURP, no change

in the cost to the MBS is applied for patients who switch from TURP to PUL (i.e. #2 in Table 19).

The pre-ESC response clarified that the ADAR assumed the highest possible number of PUL procedures - all claims on MBS Item 36811 - CYSTOSCOPY with insertion of urethral prosthesis were all for PUL. The applicant noted that the commentary questioned the number of claims estimated. Moreover, the commentary stated that targeted consultation feedback from Private Healthcare Australia indicated that sales of the prostheses is approximately $2.7 million at present with the average number of prostheses implanted being 3.1 at a cost of $712 per prosthesis. The applicant noted that $2,700,000 divided by $712 divided by 3.1 gives a patient population of 1223 and that the ADAR used a patient population of 1230.

14. Key issues from ESC for MSAC

ESC key issue	ESC advice to MSAC
Current MBS item encompasses a range of services	A new MBS item specific to prostatic urethral lift may be appropriate if the fee increase is supported by MSAC.
PUL may not be non-inferior to TURP	The key direct comparative study, BPH6, used a composite outcome which biases the results against TURP. However PUL was statistically and clinically inferior to TURP on the clinically relevant measures of effectiveness: International Prostate Symptom Score and peak urine flow rate. For the safety outcomes relating to surgical outcomes and functioning, PUL has superior safety to TURP, particularly on measures of ejaculation. However, the MBS already has previously noted that retrograde ejaculation is not considered a serious complication of TURP.
Non-inferiority claim vs VLAP is uncertain and not well supported.	As there is no direct evidence comparing VLAP to PUL, the claim of non-inferiority of PUL to VLAP rests on the MSAC advice that VLAP is non-inferior to TURP. As the claim of non-inferiority to TURP is not well supported, neither is the claim of non-inferiority to VLAP.
PUL may cost more than TURP or VLAP	Overall The cost of reintervention for PUL is underestimated The cost of PUL may be underestimated due to a lower number of prostheses used (4) than in the BPH6 trial that was used as the basis for the non-inferiority claim (4.7) Versus TURP the inclusion of major complications costs for TURP only where operative complications did not significantly differ between PUL and TURP in the BPH6 study; the cost weight used to estimate the cost of major complications was outdated and overestimated the weighted cost the cost of TURP disposable loops was omitted ESC agreed the estimated length of hospital stay (2.56 days) for TURP is likely reasonable. Versus VLAP The cost of VLAP may be an overestimation due to the assumed capital and maintenance cost of $1,271.19 per procedure The assumption of a longer length of hospital stay with VLAP (2 days) relative to PUL (1 day) was not justified.

ESC key issue	ESC advice to MSAC
Financial estimates uncertain	The ADAR assumes that with the proposed fee increase, a proportion of patients would switch from TURP to PUL. However, the ADAR has not considered that some of these TURP services will be displaced, rather than replaced by PUL, as some patients will require subsequent reintervention by TURP. No change in the use of VLAP was assumed. The ESC considered the costs to the MBS were likely underestimated by the applicant.

ESC discussion

ESC noted that this application was a request to correct a claimed fee discrepancy (by seeking a fee increase of 250%) for prostatic urethral lift (PUL), following the March 2019 MSAC recommendation to increase the fee for an alternative procedure – visual laser ablation of prostate (VLAP) [Application 1518].

ESC noted the consultation feedback from two professional groups, which supported the short-term benefits of PUL (a minimally invasive procedure resulting in reduced risks to sexual outcomes), but that these professional organisations also acknowledged the lack of longer-term clinical effectiveness and safety information. ESC noted there was no consumer feedback.

ESC agreed with the commentary that PUL would require a new Medicare Benefits Schedule (MBS) item number if the fee increase was supported, as it is currently being billed under MBS item 36811 for cystoscopy with insertion of urethral prosthesis, and this is a generic MBS item that covers a number of procedures.

The ESC advised MSAC should consider whether any new MBS item descriptor for this procedure should include the following clinical criteria in addition to describing the procedure as "CYSTOSCOPY with insertion of urethral prostheses for the treatment of BPH in men"

- Aged > 50 years;
- IPSS > 12, noting this would allow patients with less severe symptoms of benign prostatic hyperplasia (BPH) to be eligible for the procedure;
- Prostate Volume < 80 mL in line with in line with international guidelines and the applicant's own website for UroLift®; or <100 mL in line with TGA approval.

The ESC noted that MSAC had considered whether to include patient eligibility criteria in the MBS item for VLAP (level of symptoms, prostate size, use of anticoagulants) during its review of the fee for that procedure in March 2019 [MSAC 1518]. On that occasion, MSAC advised against including patient eligibility criteria in the item description.

ESC agreed that transurethral resection of the prostate (TURP) and VLAP are appropriate main comparators for PUL.

ESC noted the commentary suggested PUL could also be compared with TUMT or TUNA but agreed these procedures are rarely claimed in contemporary Australian practice so these comparisons would not be informative for MSAC. On the other hand, a comparison with transurethral water ablation (TUWA) may be informative for MSAC as the use of this procedure is growing and an application seeking on-going subsidy for TUWA is also being considered at the July 2020 MSAC (see MSAC application 1586).

ESC noted the safety and effectiveness comparisons for PUL with TURP or VLAP were primarily informed by two clinical studies: BPH6 and GOLIATH.

ESC agreed with the commentary's assessment that PUL's safety was superior to TURP based on the BPH6 study. ESC highlighted that the ADAR did not include any studies directly, or indirectly, comparing PUL to VLAP. Thus, ESC could not comment on the comparative safety of PUL with VLAP.

ESC acknowledged the uncertainty in the claim of non-inferior effectiveness claim when comparing PUL with transurethral resection of the prostate (TURP), as the only direct randomised trial, BPH6, was sponsored by UroLift® and had as its primary outcome, a composite measure that was made up of five safety-orientated endpoints and one efficacy-oriented endpoint, which likely biased the study against TURP. However, the comparative effectiveness data from this study favoured TURP with the 24-month results for IPSS and Qmax both showing clinically and statistically significant differences in favour of TURP.

ESC noted the re-intervention rate in the BPH6 study at 2-years was 13.6% for PUL and 5.7% for TURP (see Table 5). The ESC considered the observed difference in re-intervention rate also supports a conclusion of superior effectiveness for TURP over PUL.

The ESC noted that in the pre-ESC response, the applicant re-iterated that the BPH6 study concluded that PUL was clinically non-inferior to TURP using a composite endpoint. However, ESC considered this conclusion was not well supported by the results for other outcomes as described above.

The ESC also noted the applicant's pre-ESC claim that since the conclusion of the GOLIATH study was that VLAP was non-inferior to TURP, and there are no studies directly comparing PUL to VLAP, it is reasonable to conclude PUL is non-inferior to VLAP in terms of effectiveness. However, as ESC considered the claim that PUL is non-inferior in terms of effectiveness to TURP cannot be supported for reasons described above, it also follows that the claim that PUL is non-inferior to VLAP cannot be supported.

ESC noted a number of issues with the economic analysis presented by the applicant, including:

- The use of the cost of reintervention for one year only (underestimates cost of PUL)
- The assumption that an average of 4 devices will be used in each procedure when the BPH6 study used 4.7 (underestimates cost of PUL)
- the inclusion of major complications costs for TURP only, when operative complications did not significantly differ between PUL and TURP in the BPH6 study (overestimates cost of TURP)
- the cost of TURP disposable loops was omitted (underestimates cost of TURP)
- The inclusion of a very large capital and maintenance cost in the costings for VLAP (overestimates the cost of VLAP)
- The assumption that VLAP will require an average of 2 days of hospitalisation whereas PUL will require an average of 1 day of hospitalisation (overestimates the cost of VLAP).

However, ESC agreed that:

- The submission's assumption of an average of 2.57 days hospital for TURP is reasonable
- The submission's assumption of no handling fee for prosthetic devices is appropriate.

ESC noted that the applicant had conducted limited sensitivity analyses, and acknowledged the attempt to perform parameter testing using a stepped approach in the commentary.

The ESC noted the outcomes of a revised multi-variate analysis addressing the issues described above is presented in Table 18. The ESC noted that this revised analysis suggests PUL is more expensive than either TURP (by up to $615.65) or VLAP (by up to $2,269.70).

ESC advised that overall, the clinical and economic information presented in the submission and evaluation report, suggests that PUL is dominated by TURP and VLAP (i.e. PUL is less effective and more expensive). ESC noted that PUL is a non-invasive procedure compared with TURP and other ablative procedures, but did not consider the request for a fee increase to be justified by the evidence.

ESC advised the MSAC may wish to recommend the Prosthesis List Advisory Committee conduct a review of the price of the prosthesis used in PUL.

ESC noted the application estimated the financial impact to the MBS by using a modified market share approach, using the cost of current services under MBS item 36811 and an estimate of the proportion of future TURP patients that will instead undergo PUL. However, ESC also noted that the assessment report did not consider the additional cost to the MBS and to health budgets of the prosthesis from switching to PUL and the additional costs of re-intervention.

ESC acknowledged that some men may prefer PUL to TURP to maintain ejaculatory function, but queried whether PUL is a substitute for TURP for all of these patients, or if it only serves to delay TURP. ESC considered this to be important for the financial analysis, as patients requiring TURP as a re-intervention procedure after PUL would have long-term impacts for MBS costs that the applicant has not adequately accounted for.

ESC noted the pre-ESC response considered the estimate that 1230 (Table 19) of the current claims under MBS item 36811 relate to PUL is supported by the feedback from Private Healthcare Australia that sales of the prostheses are currently approximately $2.7 million. The applicant notes that $2.7 million divided by the $712 price of a PUL device, divided by an average 3.1 devices per procedure, gives a patient population of 1223 and that the application used a patient population of 1230. However, in another part of the pre-ESC response, the applicant contends that more than 3.1 PUL devices will be used on average. ESC noted that if the applicant's calculation is re-done assuming an average of 4 or 4.7 devices per procedure, then the number of patients undergoing PUL becomes 948 and 807, respectively.

Overall, the ESC considered the costs to the MBS to be underestimated by the application.

15. Other significant factors

Nil

16. Applicant comments on MSAC's Public Summary Document

The sponsor is concerned that the deferred MSAC decision, pending a review of the fee for all MBS listed treatments for BPH, allows the on-going perverse incentive against surgeons using the prostatic urethral lift (PUL) procedure due to the current low fee rather than clinical effectiveness. Clinical evidence presented in Application 1612 supports a substantial increase in the current MBS fee of $333.50 for PUL especially relative to the MBS fee of

$1,074.70 for the main comparator, TURP, and the alternative comparator VLAP. PUL is an important alternative for the treatment of BPH since it is not only minimally invasive but unlike the comparators, involves no cutting, heating or removal of prostate tissue. Additionally, many men require the advantages of PUL, namely far more rapid recovery, fewer serious adverse effects and preservation of sexual function.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website