NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Assessment report overview

GreenLight XPS 180 W for benign prostatic hyperplasia (BPH)

This assessment report overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It includes key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the Committee may wish to discuss. It should be read along with the sponsor’s submission of evidence and with the EAC report. The overview forms part of the information received by the Medical Technologies Advisory Committee when it develops its recommendations on the technology.

Key issues for consideration by the Committee are described in section 6, following the summaries of the clinical and cost evidence.

This report contains information that has been supplied in confidence and will be redacted before publication. This information is highlighted in yellow. This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies
- Appendix C: Comments from patient organisations
- Appendix D: Additional analyses carried out by External Assessment Centre
1 The technology

GreenLight XPS (Boston Scientific) is intended to treat benign prostatic hyperplasia (BPH) using a procedure called photoselective vaporisation of the prostate. The procedure involves delivering a laser through a cystoscope to vaporise extra prostate tissue, leaving a clear urethral channel. In ‘coagulation’ mode, GreenLight XPS can also seal (cauterise) any bleeding vessels which result from photoselective vaporisation of the prostate.

The procedure can be done either as a day case or on an inpatient basis. Using GreenLight XPS requires training and a mentorship scheme is in place within the NHS.

The GreenLight laser operates at a shorter wavelength (532 nm) than other laser systems used to treat BPH. The company claims that shorter wavelength light is more easily absorbed by oxyhaemoglobin (in blood and tissue), which 'vaporises' the tissue, leaving no fragments behind. GreenLight XPS also uses a proprietary MoXy laser fibre, which is actively cooled using a saline flow to improve fibre reliability.

Since its introduction in 2005, the GreenLight console and associated fibres have been upgraded, resulting in the power of the laser being increased. This allows procedures to be done on larger prostates in shorter timescales. The first clinical studies used an 80 W system; this was then upgraded to a 120 W system (GreenLight HPS) and a further upgrade in 2010 introduced the GreenLight XPS (Xcellerated performance system), the 180 W system in current use. The 180 W system also incorporates improvements to the design of the laser fibre, allowing the use of 1 fibre per patient, because laser fibre degradation was an issue in earlier versions.

The GreenLight XPS 180 W console is a class IIB device, and the MoXy disposable laser fibre is a class IIA device. The first version of Greenlight was CE marked in 2005; Greenlight XPS and the MoXy fibre were CE marked in 2010.
2 Proposed use of the technology

2.1 Disease or condition

Benign prostatic hyperplasia (BPH) is the most common cause of lower urinary tract symptoms (LUTS), although the two are not synonymous. As the prostate becomes enlarged, bladder outflow may be obstructed. Surgical treatments seek to improve symptoms by removing excess prostate tissue. LUTS can be categorised into voiding, storage and post-urination symptoms. Voiding symptoms are the most common, such as straining and hesitancy, but storage symptoms (such as frequency and urgency incontinence) are often more problematic.

Both storage and voiding symptoms are common in patients with LUTS secondary to BPH. Increasingly severe LUTS are also associated with erectile and ejaculatory dysfunction.

2.2 Patient group

The prevalence of BPH increases with age. The first pathological signs of BPH are seen in men aged 31 to 40 years, although prevalence is typically only 8%. This rate increases rapidly with age: around 60% of men aged 60 years or older and over 80% of men aged 70 or older will experience some degree of prostate enlargement (McVary 2006).

Moderate to severe LUTS (classified using the International Prostate Symptoms Score) are present in about 40% of men older than 50 years, rising to 90% of men older than 80 years. Moderate to severe LUTS are estimated to affect up to 3.4 million men in the UK (Rees 2014), and Hospital Episode Statistics indicate that over 23,000 transurethral resection of the prostate (TURP) operations were performed in England and Wales in 2014/15.
2.3 **Current management**

Current management for men with LUTS is outlined in NICE’s guideline on lower urinary tract symptoms and in the NICE pathway on lower urinary tract symptoms in men.

Surgical options recommended by NICE include:

- monopolar or bipolar TURP
- transurethral vaporisation of the prostate (TUVP)
- holmium laser enucleation of the prostate (HoLEP)
- transurethral incision of the prostate (TUIP; only in prostates smaller than 30 ml)
- open prostatectomy (only in prostates larger than 80 ml).

Minimally invasive treatments such as transurethral needle ablation (TUNA), transurethral microwave thermotherapy (TUMT), high-intensity focused ultrasound (HIFU), transurethral ethanol ablation of the prostate (TEAP) and laser coagulation are not recommended by the NICE guideline. Laser vaporisation techniques (such as GreenLight XPS PVP) should only be used as part of a randomised controlled trial that compares these techniques with TURP. NICE has also recommended the UroLift prostatic urethral lift system as an alternative option (see NICE medical technologies guidance on UroLift for treating lower urinary tract symptoms of benign prostatic hyperplasia).

2.4 **Proposed management with new technology**

GreenLight XPS would be used as a direct alternative to bipolar or monopolar TURP, HoLEP or TUVP at the surgical stage of the care pathway. The device may also be an option for people at particular risk of bleeding complications with surgical treatment.

2.5 **Equality issues**

GreenLight XPS is indicated primarily for use in men over the age of 50 years. However, this is a function of the clinical condition for which the technology is
indicated and is not likely to be considered an equalities issue. LUTS secondary to BPH are more prevalent in black men than in men who are white or of Asian family origin. This is also a function of the clinical condition, not of the technology itself.

Laser vaporisation technology such as GreenLight XPS may reduce the risk of bleeding, and so allows transurethral surgery to be done in previously excluded groups (such as people taking anticoagulant therapies, people with bleeding disorders and people whose beliefs prevent them from accepting blood transfusions. Many of these people are covered under the 2010 Equality Act.
3 Company's claimed benefits

The benefits to patients claimed by the company are:

- GreenLight XPS laser therapy can be done in a hospital day case or inpatient setting. Patient benefits include:
  - lower likelihood of hospital readmission within 30 days
  - quicker return to normal activity
  - reduced stress and anxiety, as typically no overnight stay is required
  - reduced pain (dysuria), improving quality of life.
- Other benefits to the patient include:
  - shorter duration of catheterisation
  - can be used in patients on anticoagulants or who have prostates of over 100 ml.
- Using GreenLight XPS carries a reduced risk of:
  - capsular perforation
  - excessive or severe bleeding
  - transurethral resection of the prostate (TURP) syndrome.

The benefits to the health system claimed by the company are:

- GreenLight XPS is a cost-effective alternative to TURP, providing similar benefit at a lower cost to the health system by:
  - being done in a day-case setting
  - reduced length of stay in hospital
  - lower rates of adverse events needing surgical, endoscopic or radiologic intervention
  - lower rates of hospital readmission within 30 days of surgery.
# 4 Decision problem

## Table 1 Summary of the decision problem

<table>
<thead>
<tr>
<th>Population</th>
<th>People with urinary outflow obstruction secondary to BPH in whom surgical intervention is indicated especially those with larger prostates (≥30 ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>GreenLight XPS 180 W Photoselective Vaporisation of the Prostate (PVP)</td>
</tr>
</tbody>
</table>
| Comparator(s) | • Monopolar transurethral resection of the prostate (TURP)  
• Bipolar TURP  
• Holmium laser enucleation of the prostate (HoLEP)                                                                 |
| Outcomes | **Patient outcomes**  
• symptoms of BPH (International Prostate Symptom Score [IPSS] and International Prostate Symptom Score Quality of Life [IPSS-QOL], change in prostate volume, maximum flow rate [Qmax], post-void residual volume [PVR])  
• duration of catheterisation  
• rate of dysuria (pain)  
• quality of life  
**System outcomes**  
• length of hospital stay  
• frequency of completion as a day-case  
• rate of re-admission  
• procedural blood loss and blood transfusion requirement  
**Adverse effects**  
• rate of TUR syndrome  
• rate of capsular perforation  
• device-related adverse events |
| Cost analysis | **Comparator(s):**  
• monopolar TURP  
• bipolar TURP  
• HoLEP  
Costs will be considered from an NHS and personal social services perspective.  
The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared.  
Monopolar TURP and bipolar TURP should be included as in-patient procedures in the cost model to reflect the setting they are routinely used in the NHS.  
Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which |
different numbers and combinations of devices are needed.

### Subgroups to be considered
- High risk patients, including those with pacemakers or defibrillators and those at risk of bleeding sequelae (including people on anti-coagulation therapy, with a history of bleeding disorders, those with a history of atrial fibrillation, an implanted prosthetic heart valve, implanted coronary stents, patients on aspirin therapy for prior coronary events, patients with prior deep vein thrombosis [DVT] or a high risk of DVT, stroke survivors, haemophiliacs, and patients who do not wish to have blood transfusions)
- Patients with a prostate size greater than 100 ml
- Patients with urinary retention

### Special considerations, including issues related to equality
The GreenLight XPS 180 W laser system is indicated primarily for use in men over the age of 50, because this is the group in whom histological BPH is most prevalent. This is a function of the clinical condition for which the technology is indicated, and is not likely to be considered an equalities issue. LUTS secondary to BPH are more prevalent in black men than men of white or Asian origin. This is also a function of the clinical condition, not of the technology itself.

Laser vaporisation technology such as GreenLight has the potential to reduce the risk of bleeding compared with other surgical options and so allows transurethral surgery to be undertaken on previously excluded groups, such as those on anticoagulant therapies, those with bleeding disorders and those whose beliefs prevent them from receiving blood transfusions, many of whom may be covered under the 2010 Equality Act.

<table>
<thead>
<tr>
<th>Question</th>
<th>Answer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristics?</td>
<td>No</td>
</tr>
<tr>
<td>Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?</td>
<td>No</td>
</tr>
<tr>
<td>Is there anything specific that needs to be done now to ensure MTAC will have relevant information to consider equality issues when developing guidance?</td>
<td>No</td>
</tr>
</tbody>
</table>

In its submission, the company stated that there was no variation from the scope (pages 9–10) and that the evidence submitted addressed each of the outcomes defined in the scope (page 44). The External Assessment Centre (EAC) considered that the company’s clinical evidence submitted for the primary (average-risk) population included appropriate patients and outcomes. The company submission for average-risk patients did not include evidence.
on pain, blood loss, TURP syndrome or capsular perforation, because these were not reported in the GOLIATH trial (Bachmann 2014, Bachmann 2015, Thomas 2015). The comparator for the GOLIATH trial was TURP; outcomes were not reported separately for monopolar or bipolar TURP, but the EAC considered that this was appropriate, given the clinical equivalence between these interventions.

For the high-risk subgroups defined in the scope, (people at risk of bleeding, with larger prostates or in urinary retention), the EAC stated that the submitted evidence only partially reflected the decision problem. The EAC highlighted that there was no submitted evidence on patients with prostates larger than 100 ml or patients at risk of bleeding not taking anticoagulants. The EAC felt that the patient populations in the high-risk evidence were probably appropriate to the scope, although they were poorly described in the papers. The evidence submitted by the company on high-risk populations used the older version of GreenLight HPS 120 W for patients taking anticoagulants, but the current version of GreenLight XPS 180 W for patients with larger prostates. No evidence was submitted comparing GreenLight (120 W or 180 W) with holmium laser enucleation of the prostate (HoLEP).

The company stated that the cost analysis was relevant to all groups of patients and NHS settings in England as identified in the scope (p.78, company submission). The EAC considered that the GOLIATH trial evidence used in the company’s cost model (Bachmann 2014) broadly fitted the population as defined in the scope for average-risk patients, but not for high-risk patients (p.46, assessment report). For high-risk patients, the company used additional evidence that used the 120 W system (Woo 2008).

5 The evidence

5.1 Summary of evidence of clinical benefit

The company identified 6 relevant clinical studies from 2 independent literature searches (table 2). The company specified the primary search as

Assessment report overview: GreenLight XPS 180 W for BPH
December 2015
randomised clinical trials only with GreenLight XPS 180 W in patients with lower urinary tract symptoms (LUTS) secondary to benign prostatic hyperplasia (BPH; page 19, company submission). The secondary search was for any study using GreenLight XPS 180 W, or GreenLight HPS 120 W in high-risk patients with LUTS secondary to BPH, specified as those taking anticoagulants, with prostate glands larger than 100 ml or in urinary retention.

**Primary analysis**

The company identified 45 studies from its initial search and selected 3 published reports from a single trial that compared GreenLight 180 W XPS with transurethral resection of the prostate (TURP; the GOLIATH study: Bachmann 2014, Bachmann 2015, Thomas 2015). Figure 3 in the company submission (page 20) summarises the study selection process.

The External Assessment Centre (EAC) considered the company’s search strategy to be appropriate, and identified only 1 other trial that compared GreenLight XPS 180 W with TURP (Jovanovic 2014).

The EAC considered that GOLIATH was of high quality (see table 2) and that the critical appraisal conducted by the company was appropriate (company submission, page 29). Results are summarised below and discussed in the company submission (pages 32–41) and the assessment report (table 2 and pages 19–22, 24–25).

The GOLIATH study was a multicentre European randomised controlled trial including 281 patients with BPH who were not considered to be high risk, i.e. not on anticoagulant therapy and with prostates less than 100 ml. Patients were randomised to either GreenLight XPS 180 W or TURP (monopolar or bipolar) and followed-up for 2 years, with results reported at 6 months (Bachmann 2014), 1 year (Bachmann 2015) and 2 years (Thomas 2015).

Compared with TURP, GreenLight XPS 180 W resulted in significantly shorter lengths of catheterisation (40.8 hours compared with 59.5 hours, p<0.001) and shorter lengths of hospital stay (65.5 hours compared with 96.9 hours,
However, procedures with GreenLight XPS 180 W took longer than TURP (49.6 minutes compared with 39.3 minutes, p<0.001). There were no statistically significant differences between groups in symptoms of BPH relevant to the decision problem, such as the International Prostate Symptom Score (IPSS) or the maximum urinary flow rate (Qmax). Rates of adverse events and the percentages of patients who were complication-free after 180 days were similar between groups.

Jovanovic et al. (2014) studied 62 patients with LUTS secondary to BPH in a single centre in Serbia. The study population were not on anticoagulants and had prostates smaller than 100 ml, but 11 patients had indwelling catheters. Patients were randomised to either GreenLight XPS 180 W or TURP (monopolar or bipolar not specified). Intraoperative and postoperative outcomes and adverse events were reported.

Compared with TURP, GreenLight XPS 180 W showed significantly shorter hospital stays (1.9 days compared with 4.4 days, p<0.0001) and lengths of catheterisation (1.1 days compared with 2.9 days, p<0.0001), but longer operating times (92 minutes compared with 82 minutes, p<0.01). There were statistically significantly fewer adverse events with GreenLight XPS 180 W than with TURP, including blood transfusions, capsule perforations and TURP syndrome. In both groups, IPSS and Qmax improved from baseline but no statistically significant differences between GreenLight XPS and TURP were reported.

Adverse events for average-risk populations reported in the company submission were from the GOLIATH study, with additional information on laser safety in the operating theatre. The EAC queried the FDA MAUDE database and found no unexpected levels of adverse events. Further information on adverse events and the Clavien-Dindo grading used in BPH studies are detailed in the assessment report (pages 24–25 and Appendix 1). The EAC stated that there was insufficient information from the submitted evidence to determine differences in adverse events with GreenLight XPS 180
W and TURP, because the EAC considered that the sample size of GOLIATH was insufficiently powered for these outcomes.

From all the evidence identified for the primary analysis of average-risk populations, the EAC concluded that there was sufficient information to suggest that treatment with GreenLight XPS 180 W is similar to TURP in terms of effectiveness and adverse events. The EAC also concluded that the operating time using GreenLight XPS 180 W is longer than that of TURP, but is associated with shorter durations of postoperative catheterisation and hospital stay.

**Secondary analysis**

The company selected 3 relevant published studies of GreenLight XPS 180 W XPS or GreenLight HPS 120 W in the high-risk subgroups of interest to the decision problem (Woo 2008, Woo and Hossack 2011, Chung 2012). The EAC considered these studies to be of low quality because they were all small observational case series of GreenLight devices, with no comparison with other interventions. One study was considered not relevant by the EAC, because most of the results were not stratified by high-risk subgroups (Chung 2012). Characteristics of these studies are summarised in Table 2 and described in more detail in the company submission (Table 3 and 5, pages 22–25). Results of the studies considered relevant are summarised below and discussed in the company submission (pages 34–41) and the assessment report (pages 18, 22–26).

Woo et al. (2008) studied a case series of 305 patients with BPH who had treatment with GreenLight HPS 120 W at 8 centres across 6 countries. Patients considered to be at high-risk (patients with large prostates (>80 ml), on anti-coagulants and those in urinary retention) were compared with those without high-risk factors, with a mean follow-up of 4.2 months. For all patients, clinical outcomes improved significantly from baseline (p<0.001). For those with large prostates, the only difference when compared with those with smaller prostates was in prostate volume reduction (PVR, p<0.001). There...
were no differences in outcomes for patients taking anticoagulants compared with patients not taking them. For patients with or without urinary retention, the only significant difference between groups was for Qmax (a measure of the maximum urinary flow rate: 16 ml/sec compared with 22.7 ml/sec, p<0.001). Detailed results are described in the assessment report (tables 3–5, pages 22–26).

Woo and Hossack (2011) reported a retrospective case series of 43 high-risk patients with BPH taking anticoagulants, who had the GreenLight HPS 120 W procedure at a single centre in Australia. For the whole cohort, the mean hospital stay was 32 hours. Outcomes were reported at 3 months, including a subgroup of patients with urinary retention at baseline compared with those without. There were no significant differences in outcomes between these groups except for IPSS score, which was significantly worse in patients with urinary retention than those without (6.7 compared with 12.6, p<0.01). Detailed results are shown in the assessment report (table 3, pages 22 and 25).

The EAC concluded there was insufficient information from the submitted clinical evidence to determine whether high-risk patients treated with GreenLight XPS 180 W are at a greater risk than average-risk patients. The 2 comparative case series accepted by the EAC were too small to show any notable differences in effectiveness or adverse events, and both involved an earlier version of the device, GreenLight HPS 120 W.

In its additional searches, the EAC identified 10 further studies of which 5 yielded useful information (Chen et al. 2013b, Sohn et al. 2011, Tao et al. 2013, Hueber et al. 2015, West and Woo 2015). For completeness, details of the 5 other studies are included in table 6 in Appendix D (Cakiroglu 2013, Chen 2013a, Altabay 2015, Nicholson 2015, Tam 2012).

Chen et al (2013b) reported a retrospective case series studying 132 patients having GreenLight HPS 120 W in Taiwan, who were divided into 4 high-risk subgroups (aged >80 years, prostate size >80 ml, high anaesthetic risk, taking...
anticoagulants). Patients taking anticoagulants (n=21) and with larger prostates (n=32) were compared with patients without high-risk factors (n=72). There were no significant differences reported in IPSS, quality of life score, Qmax or PVR for the anticoagulant group or larger prostate group compared with the group without risk factors. For the anticoagulant group, hospital stays and length of catheterisation were significantly longer than the group without risk factors (2.3 days compared with 1.7 days, p=0.033 and 28.8 hours compared with 19.1 hours, p=0.045). The larger prostate group had significantly longer operation times (35.5 minutes compared with 29.7 minutes, p=0.022), hospital stays (2.5 days compared with 1.7 days, p=0.01) and length of catheterisation (30.8 hours compared with 19.1 hours, p=0.021) than the group without risk factors. No patients were given blood transfusions in any group and there were no significant differences in postoperative complications between groups, except for more urinary tract infections in patients taking anticoagulants (3 compared with 1, p=0.035).

Sohn et al. (2011) describes a retrospective study of 60 patients having Greenlight HPS 120 W in Korea, comparing 30 patients who stopped anticoagulants before surgery with 30 patients who continued anticoagulants. The operation time in the stopped group was not significantly longer than the continued group (24.9 minutes compared with 16.9 minutes; p=0.628). There were no statistically significant differences between groups in IPSS, QoL or PVR at 3-month follow up and no patients in either group developed complications.

Tao et al. (2013) describes a prospective study of 188 high-risk patients having GreenLight 120 W in China. A subgroup taking anticoagulants (n=45) were compared with the entire high-risk cohort (n=188), but statistical analysis was not done. Perioperative outcomes were similar between the anticoagulant group and the entire cohort, with comparable operation times (49.5 minutes compared to 50.8 minutes), admission times (4.5 days for both) and lengths of catheterisation (1.8 days compared to 1.9 days). Follow-up results were not reported for the anticoagulant group.
Hueber et al. (2015) was a large retrospective study of 1196 patients having GreenLight XPS 180 W in 6 centres in Canada, the US, France and England. Subgroups of patients with larger prostates (>80 ml, n=741) were compared with those with smaller prostates (<80 ml, n=387) with a 2-year follow-up. The population included some patients on anticoagulants and in urinary retention. Perioperative results in groups with larger versus smaller prostates showed that operation times and length of catheterisation increased with prostate size (80 minutes compared with 45 minutes, p<0.01; 34 hours compared with 26 hours, p<0.01), but mean hospital stay was 24 hours in both groups. There were no significant differences in adverse events, apart from a greater conversion to TURP in the larger prostate group (8.4% compared with 0.6%, p<0.01). Improvements in IPSS, QoL, Qmax and PVR from baseline were not significantly different between groups.

West and Woo (2015) describe a retrospective study of 137 patients having GreenLight XPS 180 W at a single centre in Australia, who were divided into subgroups according to prostate size: <40 ml (n=27), 40–79 ml (n=56), 80–119 ml (n=38), >120 ml (n=22). Apart from an increase in operating time with prostate size (p<0.01 between groups), there were no statistically significant differences across groups in reported outcomes, including duration of catheterisation, length of hospital stay, incidence of adverse events and proportion discharged home catheter-free within 24 hours.

Taking all evidence together, the EAC maintained there was insufficient information to know whether there are equivalent peri- and postoperative outcomes, effectiveness or rates of adverse events in high-risk patients compared with average-risk patients when using GreenLight. The EAC highlighted a lack of direct head-to-head evidence comparing GreenLight XPS 180 W with HoLEP, the appropriate comparator for high-risk patients. Although neither the company nor the EAC identified any head-to-head evidence for GreenLight XPS 180 W and HoLEP, the EAC found 1 additional trial that compared GreenLight XPS 180 W and HoLEP but using GreenLight for vapo-enucleation instead of standard vaporisation techniques (Elshal}
2015). The EAC also identified a randomised controlled trial which compared GreenLight HPS 120 W with HoLEP (Elmansy 2012). These 2 additional studies are discussed below and in more detail in the assessment report (Table 8 and pages 33–35).

Elshal et al. (2015) describes a randomised controlled trial of 103 patients with LUTS secondary to BPH, randomised to have vapo-enucleation with GreenLight XPS 180 W or HoLEP performed by a single surgeon in Canada. The population included high-risk subgroups, including patients taking anticoagulants, in urinary retention and with larger prostates. Peri- and postoperative outcomes at 12 months did not differ significantly between GreenLight XPS and HoLEP, apart from Qmax (18.5 ml compared with 31.1 ml, p=0.01) and the percentage of patients with a hospital stay of more than 1 night (23.5% compared with 6.4%, p=0.02). GreenLight XPS 180 W vapo-enucleation is a different technique to photoselective vaporisation and is described as ‘off-label’ use by the company, so this study was not included in their submission. The EAC included this study in its assessment because they state it is the only direct evidence available comparing GreenLight XPS 180 W with HoLEP. However, expert opinion sought by the EAC highlighted that using GreenLight XPS 180 W for vapo-enucleation is a very different and new technique that does not represent standard care in the NHS (see the EAC correspondence log).

Elmansy et al. (2012) studied 80 patients with LUTS secondary to BPH with prostates larger than 60 ml, randomised to GreenLight HPS 120 W or HoLEP in a single centre in Canada. The population included high-risk patients taking anticoagulants, in urinary retention and with large prostates (62–160 ml). Results showed no difference in operative time or length of catheterisation between groups. Functional outcomes at 12 months were similar for GreenLight HPS 120 W and HoLEP, apart from Qmax (24.1 ml compared with 30.5 ml, p=0.02) and PVR (64.8 ml compared 29.4 ml, p=0.02). Adverse event rates were similar between groups, except for 8 cases with GreenLight 120 W that required conversion to TURP or HoLEP because of bleeding or
inadequate tissue removal. No blood transfusions were needed in either group.

The company did not include this study in its submission because it used the earlier 120 W version of the device, which the company claims is technically different to GreenLight XPS (180 W) in terms of rate and volume of tissue removal, and the ability to coagulate bleeding vessels. Additional work by the EAC included a comparative review of GreenLight XPS 180 W and GreenLight HPS 120 W: results are shown in Appendix D and the assessment report (pages 35 and 87–89). In summary, the EAC concluded that operating times and mean hospital stays tend to be shorter with GreenLight XPS 180 W compared with GreenLight HPS 120 W. Fewer laser fibres tend to be used with GreenLight XPS 180 W, but it also carries a slightly greater risk of capsular perforation. At follow-up, there appeared to be few consistent differences between the 2 devices, but the numbers of events were low for both treatments, precluding firm conclusions.

Further work by the EAC included a critical appraisal of a systematic review of HoLEP compared with TURP (Li 2014): results are shown in table 9 of Appendix D. In summary, a meta-analysis of 8 randomised controlled trials showed that HoLEP operations take longer than TURP, but the average length of hospital stay is shorter. There are few statistically significant differences in postoperative complications, but HoLEP has statistically significantly better curative outcomes at 12-month follow-up compared with TURP.

**Summary of clinical evidence**

The EAC concluded there was sufficient evidence to suggest that treatment with GreenLight XPS 180 W is clinically similar in effectiveness and in terms of adverse events to TURP for average-risk patients. The operating time for GreenLight XPS 180 W is longer than for TURP, so it is likely that fewer cases will be treated if no additional operating theatre list time is available. However, because average lengths of catheterisation and hospital stays are shorter with
GreenLight XPS 180 W than with TURP, postoperative recovery is quicker. The EAC therefore concluded that there may be scope for more efficient hospital bed use with GreenLight XPS 180 W than with TURP.

For high-risk subgroups (that is, patients taking anticoagulants, with larger prostates and in urinary retention), the EAC concluded there was insufficient evidence to determine whether there are equivalent outcomes with GreenLight XPS 180 W and HoLEP. The case series in these high-risk subgroups had sample sizes too small to show any notable differences in effectiveness or adverse events.

Neither the company nor the EAC did any evidence synthesis or meta-analysis, but the EAC considered that this would have been inappropriate given the amount of evidence found in the primary searches (only 2 trials) and the study designs in the secondary searches (case series).
### Table 2 Clinical studies selected by the company

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design (country)</th>
<th>Population</th>
<th>Intervention versus comparator</th>
<th>Outcomes considered</th>
<th>EAC comments on study</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary search (Greenlight XPS 180 W RCTs)</strong></td>
<td></td>
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</table>
| Bachmann et al 2013: GOLIATH (6 months) | RCT in 29 centres in Europe (9 European countries) | Men aged 40-80 years, with LUTS due to BPH, prostate volume <100 ml, and not on ACO | GL XPS 180 W (n=139) vs. TURP (monopolar or bipolar) (n=142) | • IPSS  
• Length of catheterisation  
• Length of hospitalisation  
• Time to stable health  
• Freedom from complications at 180 days | Blinding of study participants not possible due to the laser safety equipment for GL, but AE adjudication committee was blinded. Allocation by sealed envelope not computerised off-site allocation. ITT analysis for IPSS and Qmax by excluding patients (modified ITT) and imputing their endpoint with baseline observation - the ITT analyses and by treatment were in agreement. The implications of a 1-tailed statistical analysis were not discussed. Sample size was insufficient to demonstrate significance of any differences in the AE rate between GL and TURP. Study excluded high-risk groups. Data on ethnicity not recorded. |
| Bachmann et al 2014: GOLIATH (1 year) | As above | As above | As above | As above at 1 year | |
| Thomas et al 2015: GOLIATH (2 years) | As above | As above | As above | As above at 2 years plus: • IPSS-QoL  
• Qmax  
• PVR  
• PV (TRUS)  
• PSA  
• PROMs for health, urinary incontinence and satisfaction | |
| **Secondary search (GreenLight 180 W or 120 W in high risk subgroups)** | | | | | |
| Woo et al, 2008 | Prospective single-arm | Patients with LUTS due to BPH (n=305) | Greenlight HPS 120 W – follow-up for | • PV  
• Qmax | Observational study with no intervention comparator. |

Assessment report overview: GreenLight XPS 180 W for BPH
December 2015
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<tr>
<th>Study</th>
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</thead>
</table>
|       | observational cohort study in 8 centres (UK, Spain, CH, DE, USA, Aus) | including patients on ACO (n=67), in urinary retention (n=63) and with prostates >80 ml (n=52) | 11 months (no comparator) | • PV  
• IPSS | |
| Woo and Hossack 2011 | Retrospective observational database review in 1 centre (Aus) | Patients who received intervention on ACO (n=43), including patients on urinary retention (n=17) | Greenlight HPS 120 W – follow-up for 3 months (no comparator) | • IPSS  
• QOL  
• Qmax  
• PVR | Observational study with no intervention comparator. No details of inclusion and exclusion criteria given. Background characteristics not reported – no information on confounding factors available, so unclear if subgroups are comparable. |
| Chung et al, 2012 | Retrospective observational cohort study in 6 centres (Aus) | Patients who received intervention (n=85), including patients on ACO (n=37) and patients with urinary retention (n=17) | Greenlight XPS 180 W follow-up for 3 months (no comparator) | • Operating time (min)  
• Laser time (min)  
• Energy usage (kJ)  
• Post-operative duration of catheterization (hours)  
• Post-operative duration of hospital stay (hours) | No intervention comparator. Baseline characteristics not reported, so information lacking on confounding factors so unclear if subgroups comparable. Most results not stratified by high-risk groups, just on entire cohort, so results not useful for estimating the effect of GL in a high-risk group. |

Abbreviations: ACO, anticoagulants; AE, adverse events; Aus, Australia; BPH: benign prostatic hyperplasia; CH, Switzerland; DE, Germany; GL, GreenLight; IPSS: International Prostate Symptom Score; ITT, intention-to-treat; LUTS, lower urinary tract symptoms; PROM, patient-reported outcome measures; PSA, prostate-specific antigen; PV, prostate volume; PVR, Post-void residual urine volume; Qmax: max urinary flow rate; QoL: quality of life; RCT: randomised controlled trial; TRUS, transrectal ultrasound; TURP: transurethral resection of the prostate.

Assessment report overview: GreenLight XPS 180 W for BPH
December 2015
5.2 Summary of economic evidence

The company identified 2 published cost-effectiveness studies from its literature search, both of which compared GreenLight XPS 180 W with TURP (Thomas 2015a and Benejam-Gual 2014; see figure 23 and table 9 in the company submission). The EAC identified no further studies, but highlighted that the company did not perform searches to identify resource measurement or valuation.

Thomas et al. (2015a) included data from the GOLIATH study. The authors used a Markov model with a lifetime horizon to estimate quality-adjusted life years (QALYs) gained and costs from a UK NHS perspective. Sensitivity analyses were mixed, but using GOLIATH data meant the costs were almost equal for GreenLight XPS 180 W and TURP. If more than 32% of patients were discharged as day cases with GreenLight XPS 180 W, it became cost-saving. Therefore, the main cost driver was the proportion of procedures carried out as day cases. However, the EAC found several issues with the accuracy of the input parameters used. Moreover, the capital costs of the GreenLight equipment were not included, only the cost of the fibres, which makes the findings relevant only if the NHS incurs no capital costs in adopting the technology. This study was the only published economic study used to inform the company’s de novo model.

Benejam-Gual et al. (2014) used retrospective data from 79 patients in 4 centres in Spain to estimate the direct costs of procedures and complications over a 3-month time horizon. The EAC identified serious uncertainties with the resource costs and lengths of stay. Despite these limitations, the EAC considered that the study showed that GreenLight XPS 180 W may be associated with shorter lengths of stay than TURP, thus may be potentially cost-saving.
### Table 3 Economic studies selected by the company

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design (country)</th>
<th>Population</th>
<th>Intervention versus comparator</th>
<th>Outcomes considered</th>
<th>EAC comments on study</th>
</tr>
</thead>
</table>
| Thomas 2015a | State-transition Markov model with a lifetime horizon (9 European countries). Sensitivity analyses with 5 different data sources, including the GOLIATH study | Patients with BPH with a surgical indication | GL XPS 180 W versus TURP | • Procedure costs (£)  
• Costs (£) of complications, repeat procedures, managing incontinence, lack of remission  
• QALYs gained (utilities) | Some issues identified with the accuracy of some of the input parameters, such as:  
• risk ratios  
• GL capital costs  
• Probability of requiring re-operation  
GL procedure costs are unclear as cost of machine and training not included, only cost per fibre. Number of fibres not taken into account in model with GOLIATH data. Uncertainty with the assumption of >70% day cases with GL XPS 180W, as not in agreement with the GOLIATH data |
| Benejam-Gual 2014 | Retrospective direct cost analysis over 3 months (Spain) | Patients with BPH (IPSS≥15, Qmax ≤15ml/sec and PV between 40 and 80 ml) | GL XPS 180 W versus TURP | • Direct medical costs only (€) of procedure and complications, analysed in 3 phases: pre-surgical, surgical and post-surgical | Unclear on how data on resources were collected and valued.  
Average LOS shorter than observed in GOLIATH and influenced by short stays in 2 out of 4 centres.  
Exclusion criteria and statistics yielded very small errors for the costs. Patients with extreme LOS were removed as outliers. |

Abbreviations used: BPH: benign prostatic hyperplasia; GL, GreenLight; IPSS: International Prostate Symptom Score; LOS, length of stay; QALYs: quality-adjusted life years; Qmax: maximum urinary flow rate; TURP: transurethral resection of the prostate
The EAC concluded that there is potential for treatment with GreenLight XPS 180 W to be cost saving compared with TURP in average-risk patients. However, the EAC highlighted uncertainties with the available economic evidence, especially in high-risk populations, which indicated that the costs of GreenLight XPS 180 W were probably the same as TURP.

**De novo cost analyses**

The company presented 2 de novo cost analyses comparing the cost consequences of procedures using GreenLight XPS 180 W in different populations with different comparators:

- A primary analysis comparing GreenLight XPS 180 W with monopolar/bipolar TURP in an average-risk population (patients with LUTS secondary to BPH, not in urinary retention, not taking anticoagulation therapy and with prostates smaller than 100 ml).
- A secondary analysis comparing GreenLight XPS 180 W with HoLEP in a high-risk population (patients with LUTS secondary to BPH, in urinary retention, taking anticoagulation therapy or prostates larger than 100 ml).

Both cost models used the same decision-tree structure (figure 1), where patients enter the model upon surgery (either GreenLight 180 W or monopolar/bipolar TURP or HoLEP), with patients routed through 4 potential pathways. The post-treatment pathways had options to be treated as an inpatient or discharged as a day case, with further options for no additional symptoms or post-surgery complications (which may lead to readmission or no readmission). At the end point of the model, patients had no further symptoms or continued to be symptomatic. The model had a NHS perspective with a 6-month time horizon and a discount rate of 3.5%. The 6-month end point was based on expert opinion and GOLIATH (Thomas 2015), where outcomes were stable after 6 months. Details of the company model are discussed below, in the company submission (pages 54–70) and in the assessment report (pages 44–59).
Figure 1 Company cost model structure

Model clinical parameters

For the primary (average-risk) model, the clinical parameters used by the company included IPSS score, the probability of being complication-free and the proportion of adverse events, all derived from the 6-month GOLIATH study (Bachmann 2014). Mean excess bed days were 10.36 days for GreenLight XPS 180 W and 10.65 for TURP, sourced from 2014/15 NHS Hospital Episode Statistics (HES). A key clinical parameter was the probability of being discharged as a day case. The company recognised there was considerable uncertainty with this parameter, so the model allowed 4 different day-case discharge rates for GreenLight XPS 180 W informed by different sources:

- 35.96% from HES data
- 80% from a single UK hospital specialising in GreenLight
- 57.71% from French health service data
- 71.5% from the US Medicare population.

Because TURP is a mature technology, the company used the HES day-case discharge rate of 4.08% for TURP. In the absence of any UK-specific data for
HoLEP, the company assumed that the same HES day-case rate (35.96%) could be used for both Greenlight XPS 180 W and HoLEP.

For the secondary (high-risk patients) model, the only additional clinical parameter used was a 1.5% additional risk of bleeding (Woo 2008) for both GreenLight XPS 180 W and HoLEP. All other clinical parameters were the same as the primary model, which assumed that GreenLight XPS 180 W and HoLEP have the same day-case rates and efficacy and safety outcomes. The company justified this due to the absence of any head-to-head clinical trial data comparing GreenLight XPS 180 W with HoLEP.

Costs and resource use

The company calculated equipment costs for each technology (see table 4) from internal sales data (GreenLight XPS 180 W and HoLEP) and expert opinion (TURP). No capital costs were calculated for TURP or GreenLight XPS 180 W: the TURP device was assumed to be already present in NHS hospitals and the GreenLight XPS console can be provided on long-term loan if a minimum number of fibres are purchased at £550 each. For TURP consumables, it was assumed that 50% of procedures were monopolar and 50% were bipolar. For HoLEP, the company incorporated the capital costs of the laser and morcellator, based on a 5-year lifespan and treating 25 high-risk patients per year. Maintenance and training costs were assumed to be zero for GreenLight XPS 180 W and were not considered for the other comparators.

Table 4 Equipment costs of the technology and comparators

<table>
<thead>
<tr>
<th>GreenLight XPS 180 W</th>
<th>TURP</th>
<th>HoLEP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capital: £0</td>
<td>Capital: £0</td>
<td>Capital:</td>
</tr>
<tr>
<td>Consumables&lt;sup&gt;1&lt;/sup&gt;:</td>
<td>Consumables&lt;sup&gt;2&lt;/sup&gt;:</td>
<td>surgery/surgery</td>
</tr>
<tr>
<td>£550 per surgery</td>
<td>£190.50 per surgery</td>
<td></td>
</tr>
</tbody>
</table>

<sup>1</sup>Single-use laser fibre

<sup>2</sup>Assumes 50% monopolar/bipolar TURP: single-use loops and Ellik evacuator for
monopolar and bipolar TURP, glycine fluid for bipolar TURP only, saline bladder irrigation for monopolar TURP only

3 Assumes 50% multi-use/single-use laser fibres: fibre stripper and cleaver for multi-use only, morcellator blade, suction tubing, omni-jugs and Ellik evacuator for all procedures

Resource costs included hospital resource costs (procedure costs, cost per day of hospital stay, excess bed days) and the costs of adverse events (acute [classed as Grade 3, treated in hospital] or non-acute [classed as Grade 2, treated in primary care]), which were derived from national tariffs and NHS reference costs. Detailed costs are provided in tables 16–22 of the submission (pages 62–68) and the assessment report (Table 13, page 58).

The EAC considered the company’s primary model to be a fair representation of current practice; most assumptions were reasonable and the EAC found no major errors when validating the model. However, the EAC considered the parameters used for the treatment of adverse events to be unclear, as the company assumed all adverse events to be mutually exclusive. The EAC also highlighted that the 10-minute longer procedure time with GreenLight XPS 180 W compared with TURP observed in the GOLIATH study (Bachmann 2013) was not taken into account in the company model.

The EAC was not satisfied that data from the primary model were transferable to the high-risk model. The EAC felt that there was insufficient information to know whether there are equivalent operation times, lengths of stay, effectiveness or rates of adverse events with GreenLight XPS 180 W and HoLEP in patients taking anticoagulation treatment or with larger prostates. The EAC also felt there was considerable uncertainty regarding the capital costs of each technology. For GreenLight XPS 180 W, there was uncertainty regarding the hospitals’ ability to purchase the minimum number of fibres per year to qualify for a long-term loan of the device (and hold the capital costs at zero). For HoLEP, all capital costs were based on the company’s internal market data only.
Cost modelling results

Primary analysis: GreenLight XPS 180 W vs TURP in average-risk patients

The company's primary analysis found that when applying day-case discharge rates of between 36% and 80%, GreenLight XPS 180 W resulted in cost savings of between £29 and £443 per patient compared with TURP.

The company performed a deterministic sensitivity analysis in which clinical costs were varied by upper and lower limits of the 95% distribution and other costs were varied by an arbitrary 20% in each direction. The analysis determined that when the lowest day-case rate was applied, the most sensitive cost drivers were inpatient procedure costs, Greenlight XPS 180 W consumable costs and day-case procedure costs. Varying these costs by 20% resulted in GreenLight XPS 180 W being slightly more or less costly than TURP, which led the company to conclude that GreenLight XPS 180 W is cost neutral compared with TURP (see tables 25–28 and figures 27–30 in the company’s submission).

The EAC considered the parameters used for adverse events in the company’s model to be unclear, so constructed a revised model using mean inpatient costs and simplified adverse event data (figure 2). The revised model allowed for multiple adverse events per patient and used average cost estimates of treating a typical adverse event in different settings (see pages 68–70 of the assessment report).

Using the 36% day-case rate, the EAC found GreenLight XPS 180 W to be associated with a cost saving compared with TURP of £60.19 per patient. The greater savings compared with the company’s model were because of greater adverse event-related treatment costs with TURP. Although GOLIATH had shown no statistically significant difference in adverse events between GreenLight XPS 180 W and TURP in average-risk patients, the EAC’s modelled adverse event data took into account the small probability of multiple...
events per patient. As a result, slightly more adverse events occurred with TURP than with GreenLight XPS 180 W so TURP incurred a greater cost.

Figure 2 EAC’s revised model

Sensitivity analyses by the EAC determined that GreenLight XPS 180 W becomes cost saving compared with TURP in average-risk patients when the day-case rate is 30% or more. The EAC highlighted that because GreenLight XPS 180 W is not standard practice in the UK, the 2014/15 HES day-case rate of 36% may indeed be lower than that which is currently achievable, justifying the company’s analyses using higher day-case rates. Furthermore, although GOLIATH data suggest that more than 70% of GreenLight XPS 180 W patients in UK could be day cases, Thomas (2015) showed conflicting results. The EAC requested a UK-specific day-case rate from the GOLIATH study as academic in confidence data:
**Secondary analysis: GreenLight XPS 180 W vs HoLEP in high-risk patients**

The company’s subgroup analysis in high-risk patients showed that GreenLight XPS 180 W resulted in cost savings of between £591 and £1,059 per patient compared with HoLEP (see page 77 of the company submission). Because all clinical parameters were assumed to be the same between treatments, the key driver in the high-risk model was the capital costs for HoLEP (compared with zero capital costs for GreenLight XPS 180 W).

The EAC considered that there was uncertainty with the assumptions of the company’s model and the resulting cost savings in high-risk patients, but was unable to explore this further in the absence of any relevant clinical data. Accordingly, no conclusions could be drawn as the results of the EAC’s model in the high-risk population replicated that of the company model.
### Table 5. Results of the company and EAC’s primary analyses for average-risk patients

<table>
<thead>
<tr>
<th>Cost category</th>
<th>Company’s base-case estimates</th>
<th>EAC’s base-case estimates</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>GreenLight 180 W</td>
<td>TURP</td>
</tr>
<tr>
<td>Day case</td>
<td>£ 555.28</td>
<td>£ 63.00</td>
</tr>
<tr>
<td>Inpatient</td>
<td>£ 1,628.60</td>
<td>£ 2,473.46</td>
</tr>
<tr>
<td>Procedure cost (day case, inpatient, outpatient)</td>
<td>£ 2,284.88</td>
<td>£ 2,637.46</td>
</tr>
<tr>
<td>Grade 2 complications</td>
<td>£ 15.84</td>
<td>£ 11.54</td>
</tr>
<tr>
<td>Grade 3 complications</td>
<td>£ 108.11</td>
<td>£ 147.99</td>
</tr>
<tr>
<td>Capital</td>
<td>£ 0</td>
<td>£ 0</td>
</tr>
<tr>
<td>Outpatient follow-up</td>
<td>£ 101.00</td>
<td>£ 101.00</td>
</tr>
<tr>
<td>Consumables</td>
<td>£ 550.00</td>
<td>£ 145.16</td>
</tr>
<tr>
<td>Other</td>
<td>£ 0</td>
<td>£ 45.34</td>
</tr>
<tr>
<td>Total</td>
<td>£ 2,958.83</td>
<td>£ 2,987.48</td>
</tr>
</tbody>
</table>

* A minus sign indicates GreenLight 180 W is more expensive than TURP in this cost category.

** £443 (using single UK hospital day-case rate); £233 (using French day-case rate); £363 (using US day-case rate)
Summary of economic evidence

For average-risk patients, the company concluded that GreenLight XPS 180 W was cost neutral when compared with TURP. The company’s primary analysis showed that GreenLight XPS 180 W was £29 less costly, with the main cost driver being the day-case discharge rate (in agreement with published economic literature).

The EAC considered the economic evidence for the company’s primary analysis (in average-risk patients) to be robust. Its own analyses showed that GreenLight XPS 180 W was associated with a cost saving of £60 per patient compared with TURP, if the day-case discharge rate is at least 30% and GreenLight XPS 180 W is assumed to have no capital costs.

For high-risk patients, the company concluded that GreenLight XPS 180 W was cost saving when compared with HoLEP. The company’s secondary analysis showed that GreenLight XPS 180 W was £851 less costly per patient than HoLEP, with the main cost driver being the additional capital costs of HoLEP (compared with none for GreenLight XPS 180 W).

For the company’s secondary analysis (in high-risk patients), the EAC felt there was considerable uncertainty with the model’s assumptions in terms of both clinical and cost parameters. As such, the EAC concluded there was insufficient information to develop a cost case for GreenLight XPS 180 W compared with HoLEP.
6 Ongoing research

The company did not identify any ongoing studies relevant to the decision problem that were likely to report in the next year. The EAC identified 2 relevant studies in high-risk patients that are currently recruiting.

**NCT02332538** is a randomised controlled trial comparing GreenLight XPS 180 W vapo-enucleation with bipolar TURP and HoLEP in 150 patients with large prostates (80–120 ml) in a single centre in Egypt, due to complete in January 2017. **NCT02293759** is a non-randomised study comparing GreenLight XPS 180 W photoselective vaporisation with HoLEP in 60 patients with a bleeding tendency in the same centre in Egypt, due to complete in January 2016.

7 Issues for consideration by the Committee

**Clinical evidence**

- For average-risk patients, GreenLight XPS 180 W appears to have similar clinical outcomes as monopolar/bipolar transurethral resection of the prostate (TURP). It is associated with shorter hospital stays and shorter catheterisation, so there is potential for more patients to be treated as day cases with GreenLight XPS 180 W compared with TURP.
- Is the additional 10-minute procedure time reported with GreenLight XPS 180 W a concern with respect to operating lists, or is this due to a difference in surgeons’ experience and a learning curve effect, as claimed by the company?
- For high-risk patients, the EAC has stated there is insufficient evidence to determine any difference in outcomes with GreenLight XPS 180 W compared with TURP or HoLEP. Can the limited evidence base available on different versions of the device and varied study populations be used to recommend the use of GreenLight XPS 180 W with higher risk patients?
- Of the 2 studies that compared GreenLight with HoLEP, 1 used GreenLight XPS 180 W in an off-label procedure (vapo-enucleation, which expert advice indicates is not NHS practice) and another used an older version of
the device (GreenLight HPS 120 W). Is the evidence from these studies applicable to this evaluation?

**Cost evidence**

- For average-risk patients, GreenLight XPS 180 W has the potential to be cost-saving when compared with monopolar/bipolar TURP, only if:
  - the day-case discharge rate is at least 30%
  - GreenLight XPS 180 W has no capital costs (hospitals must be able to purchase a minimum number of laser fibres)
  - the additional 10-minute procedure time has no effect on the cost (it was not taken into account in the model).

Are these cost savings likely to be achieved considering these uncertainties?

- For high-risk patients, there is insufficient evidence to support the assumptions in the company’s model that result in GreenLight XPS 180 W being cost-saving when compared to HoLEP.

**8 Authors**

Abigail Stevenson, Technical Analyst
Paul Dimmock, Senior Technical Analyst

NICE Medical Technologies Evaluation Programme

December 2015
Appendix A: Sources of evidence considered in the preparation of the overview

A  Details of assessment report:


B  Submissions from the following company:

- Boston Scientific

C  Related NICE guidance


- The TURis system for transurethral resection of the prostate. NICE medical technologies guidance, February 2015. Available from: http://www.nice.org.uk/guidance/mtg23


D References


Assessment report overview: GreenLight XPS 180 W for BPH

December 2015


Appendix B: Comments from professional bodies

Expert advice was sought from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society.

Mr Raj Persad
Practising Uro-Oncology surgeon, British Association of Urological Surgeons

Mr Gordon Muir
Consultant Urologist, British Association of Urological Surgeons

Dr Andrew Dickinson
Consultant Urologist, British Association of Urological Surgeons

Mr Andrew Thomas
Senior Consultant Urological Surgeon, British Association of Urological Surgeons

Mr Neil Barber
Consultant Urologist, British Association of Urological Surgeons

Mr Stuart Lloyd
Consultant Urologist, British Association of Urological Surgeons

Mr Andrew Thorpe
Consultant Urological Surgeon, British Association of Urological Surgeons

All 7 experts had used GreenLight and all said it was at least a significant variation, with 3 experts stating that it was thoroughly novel. Two experts had undertaken research on GreenLight in the recent GOLIATH trial and one had worked as a proctor training other surgeons with GreenLight.

Experts noted a range of patient benefits around the procedure being less physically onerous and easier to complete as a day case than TURP.

Assessment report overview: GreenLight XPS 180 W for BPH

December 2015
experts cited less bleeding and shorter hospital stays as benefits. Two experts said high risk patients could benefit, with another agreeing that GreenLight had less risk of harm in patients with comorbidities. Three mentioned a quicker return to normal activities and two added that catheter times were shorter after GreenLight treatment.

- The experts agreed that shorter surgical procedures and hospital stays and the ability to treat as day cases would benefit the healthcare system. They noted fewer blood transfusions, fewer complications and a gentler operative procedure for older patients as benefits. Two experts specifically noted the avoidance of long-term catheter use in community settings, especially for older patients would be a significant benefit. One expert noted that there may also be less open prostatectomies for large prostates.

- All experts noted some training was necessary but that this was less onerous than initial training for TURP. One expert stated that the procedure was easier to train compared with HoLEP. A mentorship programme was mentioned as well as some useful simulator technology provided by the manufacturer. One expert indicated 25 mentored cases would be enough to learn the technique.

- Five experts specifically mentioned the costs of the laser fibres and three mentioned the cost of the laser machine. One expert highlighted that the cost of the laser can be offset by the fibre cost, and as a mobile unit, GreenLight can be transferred between theatres to save on costs. One expert thought the reduction in length of stay would cover capital costs, but one expressed a concern whether this would be sufficient. Another expert stated the cost of the fibres can be offset by the ability to claim day case uplift for a day case procedure. One expert mentioned “massive benefits from day cases” indicating it saved some 2.5 bed days per elective GreenLight operation. One expert said the lower rates of post-operative incontinence saved costs of incontinence treatment.
Appendix C: Comments from patient organisations

The following patient organisations were contacted and no response was received.

- Everyman
- Pelican Cancer Foundation
- Prostate Cancer Support Scotland (PCSS)
- Prostate Cancer UK (formerly prostate cancer charity)
- Prostate Help Association (PHA)
- Tackle Prostate Cancer
- Bladder and Bowel Foundation
- Urology User Group Coalition
- Men's Health Forum (MHF)
- Sexual Advice Association
- Promocon
### Appendix D: Additional analyses carried out by the External Assessment Centre

Table 6. Details of 5 additional studies on high-risk patients identified by the EAC considered non-informative

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient population</th>
<th>Country</th>
<th>Age</th>
<th>Study design</th>
<th>Sample size</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cakiroglu 2013</td>
<td>Men with BPO secondary to BPH, and on anticoagulants. Recruted between 2007-2010</td>
<td>Turkey</td>
<td>Mean age 72.8, (range 65-89)</td>
<td>Retrospective case series with follow up at 3 months</td>
<td>63</td>
<td>GreenLight 120 W</td>
</tr>
<tr>
<td>Chen 2013a</td>
<td>Men with LUTS due to BHP, at high risk including on anticoagulation, having CVD, liver or kidney dysfunction, respiratory disease or diabetes mellitus. Recruited between 2009-2011</td>
<td>China</td>
<td>Mean age 82.8, (range 70-96)</td>
<td>Prospective cohort study with follow up to 24 months,</td>
<td>120</td>
<td>GreenLight 120 W</td>
</tr>
<tr>
<td>Tam 2012</td>
<td>Patients with LUTS from BHP who had a bleeding tendency or were taking anticoagulants or antiplatelets. Recruited between 2007-2010</td>
<td>Hong Kong</td>
<td>Mean age 76, (range 62-94)</td>
<td>Prospective case series with follow up at 1,3,6 and 12 months</td>
<td>48</td>
<td>GreenLight 120 W</td>
</tr>
<tr>
<td>Altay 2015</td>
<td>Consecutive patients with LUTS due to BHP. All had prostates larger than 80mL. Recruited between 2011-2013</td>
<td>Turkey</td>
<td>Mean age 71.1, (range 49-85)</td>
<td>Prospective cohort study with follow up to 12 months,</td>
<td>68</td>
<td>GreenLight 180 W</td>
</tr>
<tr>
<td>Nicholson 2015</td>
<td>Patients with bladder outflow obstruction from BPH, with prostates larger than 100mL. Recruited between 2010-2013.</td>
<td>Australia</td>
<td>median age 70, (interquartile range [IQR] 66-79)</td>
<td>Prospective cohort study with follow up at 3 and 6 months</td>
<td>35</td>
<td>GreenLight 180 W</td>
</tr>
</tbody>
</table>
### Table 7. Baseline results of 180 W vs 120 W GreenLight laser treatment studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Power Level</th>
<th>Operating time (mins)</th>
<th>Capsular perforation</th>
<th>Mean hospital (days or hrs)</th>
<th>Mean fibre use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ben-Zvi 2013</td>
<td>120-W</td>
<td>79 (24-223)</td>
<td>1 (1.2%)</td>
<td>1.5 (0-5)</td>
<td>1.5 (1-5)</td>
</tr>
<tr>
<td></td>
<td>180-W</td>
<td>43 (15-118)</td>
<td>5 (4.1%)</td>
<td>0.3 (0-2)</td>
<td>1.0 (1-2)</td>
</tr>
<tr>
<td>Campbell 2013</td>
<td>120-W</td>
<td>65 (49.5-92)</td>
<td>0</td>
<td>19 (16-20.5)</td>
<td>ng</td>
</tr>
<tr>
<td></td>
<td>180-W</td>
<td>56 (46-78.5)</td>
<td>1 (2%)</td>
<td>18 (16.3-20.8)</td>
<td>ng</td>
</tr>
<tr>
<td>Eken 2015</td>
<td>120-W</td>
<td>58.7 (28-98)</td>
<td>ng</td>
<td>ng</td>
<td>ng</td>
</tr>
<tr>
<td></td>
<td>180-W</td>
<td>46.9 (25-95)</td>
<td>ng</td>
<td>ng</td>
<td>ng</td>
</tr>
<tr>
<td>Hueber 2013</td>
<td>120-W</td>
<td>80.4 (SD 69.5)</td>
<td>ng</td>
<td>ng</td>
<td>2.3 (SD 1.8)</td>
</tr>
<tr>
<td></td>
<td>180-W</td>
<td>53.0 (SD 30.3)</td>
<td>ng</td>
<td>ng</td>
<td>1.1 (SD 0.3)</td>
</tr>
<tr>
<td>Rieken 2013</td>
<td>120-W</td>
<td>59 (SD 36)</td>
<td>5 (6%)</td>
<td>5.9 (SD 4.0)</td>
<td>1.2 (SD 0.5)</td>
</tr>
<tr>
<td></td>
<td>180-W</td>
<td>60 (SD 37)</td>
<td>7 (9%)</td>
<td>4.3 (SD 0.8)</td>
<td>1.2 (SD 0.4)</td>
</tr>
</tbody>
</table>

### Table 8. Follow up results of 180 W vs 120 W GreenLight laser treatment studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Power Level</th>
<th>30-day readmissions</th>
<th>30-day complications – retention</th>
<th>30-day complications – incontinence</th>
<th>30-day complications – retreatment</th>
<th>Clavien Dindo grade 3 or above</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ben-Zvi 2013</td>
<td>120-W</td>
<td>5 (6%)</td>
<td>13 (16%)</td>
<td>3 (3%)</td>
<td>1 (1%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>180-W</td>
<td>5 (4%)</td>
<td>8 (6%)</td>
<td>2 (2%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Campbell 2013</td>
<td>120-W</td>
<td>ng</td>
<td>0</td>
<td>ng</td>
<td>ng</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>180-W</td>
<td>ng</td>
<td>1 (2%)</td>
<td>ng</td>
<td>ng</td>
<td>4</td>
</tr>
<tr>
<td>Eken 2015</td>
<td>120-W</td>
<td>ng</td>
<td>3 (3.4%)</td>
<td>4 (4.5%)</td>
<td>2 (2.3%)</td>
<td>ng</td>
</tr>
<tr>
<td></td>
<td>180-W</td>
<td>ng</td>
<td>3 (4.1%)</td>
<td>3 (4.1%)</td>
<td>1 (1.4%)</td>
<td>ng</td>
</tr>
<tr>
<td>Hueber 2013</td>
<td>120-W</td>
<td>ng</td>
<td>ng</td>
<td>ng</td>
<td>ng</td>
<td>ng</td>
</tr>
<tr>
<td></td>
<td>180-W</td>
<td>ng</td>
<td>ng</td>
<td>ng</td>
<td>ng</td>
<td>ng</td>
</tr>
<tr>
<td>Rieken 2013</td>
<td>120-W</td>
<td>ng</td>
<td>7 (9%)</td>
<td>ng</td>
<td>ng</td>
<td>ng</td>
</tr>
<tr>
<td></td>
<td>180-W</td>
<td>ng</td>
<td>5 (6%)</td>
<td>ng</td>
<td>ng</td>
<td>ng</td>
</tr>
</tbody>
</table>
Figure 3. Forest plot of operating time for the five 120 W vs 180 W studies

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>120W Mean</th>
<th>120W SD</th>
<th>120W Total</th>
<th>180W Mean</th>
<th>180W SD</th>
<th>180W Total</th>
<th>Mean Difference</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ben Zvi 2013</td>
<td>79</td>
<td>33</td>
<td>80</td>
<td>43</td>
<td>17</td>
<td>120</td>
<td>19.3%</td>
<td>36.00 [28.16, 43.84]</td>
</tr>
<tr>
<td>Campbell 2013</td>
<td>65</td>
<td>7</td>
<td>50</td>
<td>56</td>
<td>5</td>
<td>50</td>
<td>22.0%</td>
<td>9.00 [6.62, 11.38]</td>
</tr>
<tr>
<td>Eken 2015</td>
<td>58.7</td>
<td>12</td>
<td>88</td>
<td>46.9</td>
<td>12</td>
<td>73</td>
<td>21.6%</td>
<td>11.80 [8.08, 15.52]</td>
</tr>
<tr>
<td>Hueber 2013</td>
<td>80.4</td>
<td>69.5</td>
<td>658</td>
<td>53</td>
<td>30.3</td>
<td>359</td>
<td>20.3%</td>
<td>27.40 [21.23, 33.57]</td>
</tr>
<tr>
<td>Rieken 2013</td>
<td>59</td>
<td>36</td>
<td>80</td>
<td>60</td>
<td>37</td>
<td>80</td>
<td>16.8%</td>
<td>-1.00 [-12.31, 10.31]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>956</td>
<td></td>
<td>682</td>
<td>100.0%</td>
<td></td>
<td>16.87 [7.61, 26.14]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 100.00; Chi² = 70.78, df = 4 (P < 0.000001); I² = 94%
Test for overall effect: Z = 3.57 (P = 0.0004)
### Table 9. Meta-analysis results from HoLEP vs TURP systematic review (Li et al 2014)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Weighted mean difference (95% CIs)</th>
<th>Direction of effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of operation</td>
<td>14.19 (6.30 to 22.08)</td>
<td>Favours TURP</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>-22.25 (-29.81 to -20.68)</td>
<td>Favours HoLEP</td>
</tr>
<tr>
<td>IPSS 3 months</td>
<td>0.47 (-0.98 to 1.92)</td>
<td>NA</td>
</tr>
<tr>
<td>IPSS 6 months</td>
<td>-0.61 (-0.36 to 0.14)</td>
<td>NA</td>
</tr>
<tr>
<td>IPSS 12 months</td>
<td>-1.17 (-1.99 to -0.34)</td>
<td>Favours HoLEP</td>
</tr>
<tr>
<td>Qmax 3 months</td>
<td>3.49 (0.64 to 6.35)</td>
<td>Favours HoLEP</td>
</tr>
<tr>
<td>Qmax 6 months</td>
<td>0.62 (-0.70 to 1.94)</td>
<td>NA</td>
</tr>
<tr>
<td>Qmax 12 months</td>
<td>1.47 (0.40 to 2.54)</td>
<td>Favours HoLEP</td>
</tr>
<tr>
<td>PVR 6 months</td>
<td>-8.90 (-15.15 to -2.64)</td>
<td>Favours HoLEP</td>
</tr>
<tr>
<td>PVR 12 months</td>
<td>-15.98 (-22.50 to -9.47)</td>
<td>Favours HoLEP</td>
</tr>
<tr>
<td>Intraoperative complications</td>
<td>Blood transfusions 0.17 (0.06 to 0.47)</td>
<td>Favours TURP</td>
</tr>
<tr>
<td></td>
<td>Secondary treatment 0.57 (0.31 to 1.05)</td>
<td>Favours HoLEP</td>
</tr>
</tbody>
</table>