**Title:** PleurX peritoneal catheter drainage system for vacuum assisted drainage of treatment-resistant, recurrent malignant ascites: a NICE medical technology guidance

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**Running title:** PleurX peritoneal catheter for malignant ascites

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Key Points

- The available evidence shows high technical success for the initial PleurX placement procedure and low ongoing complication rates comparable to those of repeated large volume paracentesis (LVP).
- Patients with PleurX benefit from improved control of their symptoms and enjoy increased convenience.
- Treating malignant ascites with PleurX in the community instead of inpatient LVP can reduce costs and release bed days.
- The prevalence of recurrent, treatment-resistant malignant ascites is uncertain.
- The point in the patient care pathway at which PleurX should be considered is not clear.
Abstract

The PleurX peritoneal drainage catheter for drainage of malignant ascites in a community setting has been evaluated by the NICE Medical Technologies Evaluation Programme. This article outlines the evidence included in the Sponsor’s submission, the independent critique by the External Assessment Centre (EAC), and the recommendations made by the Medical Technologies Advisory Committee (MTAC). In accordance with the scope issued by NICE, the intervention technology was the indwelling PleurX peritoneal catheter drainage system, the comparator was large volume paracentesis (LVP; inpatient or outpatient), and the population was patients with treatment-resistant, recurrent malignant ascites. Nine studies (10 manuscripts) were identified with a total of 180 PleurX-treated patients; six were case series with more than four patients which, despite being low in the hierarchy of evidence, provided useful safety information.

Technical success of the initial PleurX placement procedure was 100% across five studies which reported this outcome. One study reported equal complication rates between patients treated with indwelling PleurX catheters (40 patients and 40 catheters) and those receiving repeated LVPs (67 patients and 392 procedures), 7.5% (3/40; 95% CI 1.6%-20%) and 7.5% (5/67; 95% CI 2.2%-15%) respectively. All remaining studies were single-arm and reported complication rates of between 0% and 59%; this wide range was largely due to variation in the definition of complications and adverse events. Using validated tools, one case series reported improvements in several ascites-related symptoms after placement of the PleurX catheter; however an overall quality of life improvement at 12 weeks was not demonstrated. Positive patient opinions relating to improved symptom control and convenience were reported in a qualitative study.

Cost analysis demonstrated that PleurX offered savings to the NHS when compared to repeated LVPs performed in an inpatient setting. This saving of £679 per patient was driven primarily by reducing hospital bed days (year 2009-10 values), but would require 23.5 additional community nurse visits. Advice from clinical experts was that additional home visits were overestimated as many patients would receive such visits regardless of whether a PleurX drain had been fitted. The model demonstrated that PleurX would be more expensive than LVP procedures performed in a setting where one or less hospital bed days were used (e.g. daycase or outpatient). There was uncertainty surrounding the number of patients for whom insertion of a PleurX drain would be appropriate as well as the point in the care pathway at which such treatment should be administered.

MTAC supported the case for adoption and considered that the available evidence showed PleurX was clinically effective, has low complication rates, can improve quality of life, and is less costly than
inpatient LVP. In the ninth Medical Technologies Guidance (MTG9) NICE recommended that PleurX peritoneal catheter drainage system be considered for use in patients with treatment-resistant, recurrent malignant ascites. (Word count 453)
1. Introduction

The National Institute for Health and Clinical Excellence (NICE) publishes evidence-based guidance on drugs, devices, procedures, and treatments, with the aim of helping the NHS, local authorities and the wider community in England and Wales to deliver patient care which is high quality and value for money. The Medical Technologies Evaluation Programme (MTEP) was established by NICE in 2009 to help adopt efficient and cost effective medical devices and diagnostics more rapidly and consistently in the NHS. MTEP is a single technology evaluation programme and will consider technologies which are: i) a medical device (as defined by the four medical device EU directives); ii) new or innovative; iii) CE-marked (or nearing this point). The Medical Technologies Advisory Committee (MTAC) comprises 25 members with a range of expertise and makes recommendations which NICE uses to produce medical technologies guidance. Only technologies which are likely to be cost saving or cost neutral, and can be evaluated as single technologies in a short time period are routed by MTAC to the medical technologies evaluation programme.

Products are notified to MTEP by the manufacturer or Sponsor, and once accepted the MTEP team produce a scope used by the company to present all of the clinical and cost evidence on the medical device, and a de novo cost model demonstrating the cost and resource implications of adopting the technology in the NHS. An independent External Assessment Centre (EAC) reviews the evidence produced by the manufacturer or Sponsor and produces a report. This EAC report, alongside the manufacturer’s evidence submission, is used by MTAC to make recommendations for NICE guidance. This article presents a summary of the EAC report for PleurX peritoneal catheter drainage system for vacuum assisted drainage of treatment-resistant, recurrent malignant ascites and the subsequent development of NICE guidance.

2. Decision Problem

2.1. Malignant Ascites

Malignant ascites is an abnormal accumulation of fluid in the peritoneal cavity as a result of cancer (1). It is caused most commonly by cancer of the ovary (36.7%) followed by pancreaticobiliary, gastric, oesophageal, colorectal, and breast cancers (2-4). Frequently, ascites is the first physical indication of intra-abdominal malignancy, and its onset is commonly associated with a deterioration in quality of life (QoL), poor prognosis, and reduced life expectancy. As large volumes of fluid accumulate in the abdomen, symptoms such as abdominal distension, anorexia, nausea, breathlessness, and poor body image perception become apparent. The prevalence of malignant ascites is unclear, although reviews by Keen et al. (5), and Becker et al. (1) report that 28,000 bed-
days were attributed to malignant ascites in England between 2007 and 2008, and malignant ascites-associated problems afflict 3.6% to 6% of patients admitted to palliative care units(6).

2.2. Current treatment
There are no current national guidelines for healthcare professionals involved in the drainage of malignant ascites. Large volume paracentesis (LVP), where accumulated fluid is drained intermittently for hours or even days using a fine tube inserted into the abdomen, is widely used to provide short term relief from the symptoms of malignant ascites. This approach is undertaken in hospital, as a day case or inpatient procedure. It is temporary solution and if ascitic fluid reaccumulates in the peritoneum the symptoms associated with malignant ascites may return. Patients will often wait until fluid accumulation is substantial to avoid frequent hospital stays, and to ensure the ascites is amenable to drainage resulting in a deterioration in their quality of life (5). Paracentesis and diuretics are the most commonly used management strategies, followed by peritoneovenous shunts, diet measures, and other modalities like systemic or intraperitoneal chemotherapy (7).

2.3. PleurX
The PleurX peritoneal catheter drainage system (manufactured by CareFusion, California, US; and distributed by UK Medical, Sheffield) comprises a catheter that is tunnelled subcutaneously where it remains indefinitely. The initial placement procedure is performed in hospital usually under local anaesthetic using ultrasound and/or fluoroscopic guidance. Patients can then return home where they or their carer are trained to perform fluid drainage as and when required. This process involves attaching the vacuum bottle to the catheter and draining no more than 2 litres of fluid from the peritoneal cavity; after drainage the bottle is disconnected, the catheter is coiled and kept underneath a dressing.

The Sponsor’s claimed benefits of PleurX compared to LVP for the treatment of malignant ascites are: i) patients will have greater flexibility and convenience to drain their ascites in a community setting; ii) more frequent drainage episodes will allow for greater control of ascites-related symptoms; iii) reduction in number of procedures and the associated risks of infection; iv) reduction in healthcare resource use, e.g. nurse and doctor time in hospital, outpatient visits, hospital bed days.

2.4. NICE’s scope
In the scope issued by NICE, the PleurX peritoneal drainage catheter was the intervention technology, the comparator being LVP performed in either an inpatient or outpatient setting. The
population was defined as patients with treatment-resistant, recurrent malignant ascites. Outcomes included procedural success, effect on symptoms (including quality of life), resource use, frequency of drainage, and adverse events. All study designs were included, as were sources such as conference proceedings, posters, and prepublication manuscripts.

3. External Assessment Centre (EAC) review

The Sponsor provided an evidence submission to NICE in line with the prescribed scope; this reviewed the clinical and cost evidence and presented a de novo cost model. Cedar, a consortium of Cardiff and Vale University Health Board (NHS) and Cardiff University, was commissioned to act as EAC on this topic.

The EAC report aimed to provide MTAC with a balanced, fair, and independent appraisal of the evidence surrounding the use of PleurX for malignant ascites (8). Broadly this involved: i) identifying any additional information not included in the manufacturer’s submission; ii) appraising the published clinical and cost evidence and where necessary presenting additional data; iii) critiquing the de novo cost model by checking inputs, assumptions, and structural integrity; iv) highlighting any key issues. The EAC was able to call upon clinical experts (Consultant Radiologists and Gynaecology Oncology Nurses) where clarification or advice on current UK practice was required.

3.1. Clinical evidence

The Sponsor presented evidence from nine studies (one of these studies was presented as two pre-publication manuscripts and a poster (9-11); the remaining eight studies comprised seven peer-reviewed publications (12-18) and one conference poster (19) (table I)). One hundred and eighty patients in total were treated with PleurX across the selected studies. All were observational studies, comprising 6 case series (n≥4 patients) (10;13;15-18), one qualitative study (19) and three case reports (11;12;14).

Technical success of the initial PleurX placement procedure (defined as successful catheter placement, withdrawal of ascitic fluid, and no procedural complications) was 100% in all studies where this outcome was explicitly reported (10;13;17;18), although there was one minor complication of epigastric vein injury reported (13). Variation in practice was identified in the use of catheter placement guidance technique, use of anaesthetic, and use of prophylactic antibiotics.

Catheter failure rates, including those requiring catheter removal or catheter intervention for restoration of patency, were reported in eight studies. In studies with more than four participants, the number of catheters requiring removal ranged from 0% to 7.5%. Reasons for removal of the
device included infection, leakage of ascitic fluid, and loculated ascites. Overall complication rates (defined as the total number of complications reported divided by the total number of patients in a study) across the studies ranged widely from 0% to 59% (table I; this variation is due largely to differences in reporting and definition of complications, e.g. some studies reported only serious complications which resulted in removal of the catheter, others reported minor complications which resolved spontaneously). Device related infections were the most common complication, with 10 cases reported across 172 patients in the case series (two required removal of the catheter, and eight were treated successfully with antibiotics. Ascitic fluid leakage, occlusions and loculations, and catheter displacement were also reported as complications. The only study to compare complication rates for PleurX and LVP reported a rate of 7.5% for both interventions (LVP 95% CI 2.2-15%; PleurX 95% CI 1.6-20%) (16). No device-related deaths were reported in any studies. Catheter patency (defined as the proportion of inserted catheters which are functioning at death, study end point, or resolution of ascites) rates ranged from 80% to 96% (from five studies where n>4; Rosenberg (2004) reported 67.5% but in this study 27.5% of patients were lost to follow-up), and mean duration of catheter survival from insertion to removal, death or study end point ranged from 52 days to 113 days (table I; weighted mean from five studies was 77.9 days). Individual catheter survival duration ranged from 1 to 365 days in studies where n>4 (a case report described one patient with a PleurX catheter in place for 18 months (12)).

Two studies, one quantitative (13) and one qualitative (19), reported quality of life (QoL) and symptom relief outcomes. Validated assessment tools (Memorial Symptom Assessment Scale, and Subjective Significance Questionnaire) showed a significant improvement of some ascites-related symptoms such as abdominal discomfort, bloating, diarrhoea, and nausea; however only 28% of patients showed an overall improvement in QoL at 12 week follow-up (13); the nature of terminal disease progression means tools designed to show week-to-week changes would understate any QoL-associated benefits of PleurX. A qualitative study showed a trend of positive attitudes amongst patients towards PleurX, specifically in the areas of increased convenience and control of ascites symptoms such as nausea, pain, mobility, and self-image (“Out of convenience I would much prefer to keep it drained all the time rather than let it build up and be uncomfortable and then have to wait on other people for a free bed...”). Some patients reported negative aspects of PleurX such as it being a constant visual reminder of their illness (19).

3.1.1. Critique and interpretation of clinical evidence

The Sponsor provided a fair quality appraisal of the selected studies, which alongside the EAC’s report highlighted the limitations of the evidence base. Specifically, the risk of bias in case series
design studies, small patient numbers, inadequate use of concurrent controls (only one study reported comparative outcomes for PleurX and LVP) (16), the retrospective nature of several studies, and variability in outcome measures (particularly inconsistent definitions of complications or adverse events). The EAC also noted that only two studies adequately reported exclusion criteria (10;13); individual characteristics such as presence of multi-loculated ascites and life-expectancy of the patient would likely have an important impact on the success of PleurX, and the appropriateness of its use.

Despite the limitations of the available evidence the EAC considered the six case series to provide valuable information on the treatment of malignant ascites with PleurX, including procedural success, catheter patency, and complication rates and types. The evidence submitted by the Sponsor indicated that the placement procedure for PleurX is safe, and there was a small amount of evidence suggesting ongoing PleurX drainage has comparable complication rates to frequent LVP procedures. PleurX offers important benefits to patients, such as avoiding hospital admissions and improved control of ascites symptoms.

3.2. Cost evidence

The Sponsor performed a robust literature search, and identified a single poster (9) and accompanying full pre-publication manuscript (10) relevant to the decision problem which the EAC independently critiqued. The EAC agreed with the issues raised by the Sponsor in relation to Mullan et al. (9;10): i) a lack of information on how costs were obtained; ii) inaccurate calculation of the cost of paracentesis resulting in a substantial overestimate of the incremental saving from PleurX; iii) costs associated with complications were omitted; iv) costs of community nurse visits for patients treated in their homes were not assessed.

The Sponsor presented an NHS-perspective de novo cost model which was well-structured and made use of the available evidence. In this analysis the cost of treating patients in the community with PleurX was compared to the cost of repeated LVP procedures in an outpatient setting and an inpatient setting. The model had a decision-tree structure with an embedded Markov time-dependent element based on decreasing survival probabilities of patients with malignant ascites with a time horizon of 26 weeks (6 months). This reflected the treatment pathway and short life expectancy of patients and appropriately no discounting was performed. Costs in the PleurX arm included an inpatient stay of one day (£312; NHS reference costs 2009-10), procedure costs (including staff; £121; from reference (10)), PleurX kits (year 2011 values), at-home nurse visits (year 2010 values (20)), and treatment of complications (year 2011 values). Costs in the LVP arm included inpatient stay (2.8 days; £312 per day; NHS reference costs 2009-10) or outpatient stay (1 day; £312
procedure costs (including staff costs; £121; from reference (10)), and treatment of complications (year 2011 costs). Comparing PleurX to repeated LVPs in an inpatient setting resulted in an incremental cost saving of £679 per patient and release of 7.4 hospital bed days per patient; this would be at the cost of 23.5 more community nurse visits to the patient’s home. When PleurX was compared to repeated outpatient LVPs, an additional cost of £1010 per patient was incurred, with a need for 23.5 extra nurse visits and the release of 1.9 hospital bed days.

The Sponsor’s one-way deterministic sensitivity analysis on all variables (±20%) identified six key drivers which were subjected to extended threshold analysis by the EAC (table II). The savings associated with PleurX when compared to inpatient LVP were strongly dependent on reducing the number of bed days in hospital. When the number of bed days required for LVP dropped below 2.1 (base case 2.8) or the cost of a bed day dropped below £220 (base case £312), the outcome switched from cost-saving to cost-incurring (table II).

Using a population estimate of 2,500 patients, the Sponsor reported an annual incremental saving to the NHS of £1,698,549 and release of 18,452 hospital bed days when comparing PleurX treatment to repeated inpatient LVP (2.8 bed days). When compared to repeated LVP with one day in hospital, PleurX would incur an additional cost to the NHS of £2,523,944, and release 4,919 bed days.

3.2.1. Critique and interpretation of cost evidence

The EAC received an executable version of the model in excel which allowed the EAC to investigate its structure and function in detail. The Sponsor’s economic model strongly suggests that when compared to LVPs performed in an inpatient setting that PleurX is cost saving and releases hospital bed days. The EAC considered that structure and inputs used in the model were mostly appropriate and in some cases were conservative (in favour of the comparator). For instance, the model estimates that 23.5 additional nurse visits would be required for each patient treated using PleurX instead of LVP; however, expert advice suggested that the Sponsor’s model may have overestimated the number of additional nurse visits required because many patients will receive community-based healthcare irrespective of having a PleurX catheter fitted. Furthermore, the NHS tariff (year 2009-10 value) used for the calculation of the excess bed day (£312) may have underestimated the true costs of an inpatient stay, and increasing this value would add to the PleurX-related savings to the NHS. There was a high degree of uncertainty surrounding the cost, type and frequency of complications in the two arms; this was reflected in several structural assumptions in the model which may not have been appropriate.
There were two significant uncertainties which impact on the population-level savings from PleurX. Firstly, the number of patients in England who could potentially be treated with PleurX was estimated by the Sponsor at 2,500, taken as 10% (the proportion of ascites cases which are due to malignancy) of 25,000 finished consultant episodes (FCEs) for procedures involving abdominal paracentesis for drainage of ascites (Hospital Episode Statistics 2008-9). The EAC considered this to be an overestimate as the number of FCEs cannot be equated to the number of patients with malignant ascites. A proportion of the abdominal paracenteses will be diagnostic, and proportion of patients with malignant ascites will not have recurrent and untreatable fluid accumulation, and therefore would not benefit from treatment with PleurX. Secondly, the proportion of patients treated in the UK using LVP in either day-case or inpatient settings was unclear. Expert opinion suggested that practice in the UK varied widely with respect to inpatient, outpatient and day-case settings; often depending on the experience and speciality of the centre. This variability also impacts on the length of inpatient stay, and consequently the potential savings associated with PleurX.

3.3. Conclusion of EAC report

Taking the limited available clinical and cost evidence together, the EAC agreed with the Sponsor that PleurX is a safe and effective alternative to LVP. Technical success was 100% and a single study provided comparative information on adverse events, in which both PleurX and LVP approaches resulted in complication rates of 7.5%. PleurX is cost-saving and releases hospital bed days when compared to inpatient LVP. PleurX was not shown to be cost-saving when compared to procedures in a setting where the number of bed days would be 2.1 or less (e.g. day case or outpatient). A small number of studies support the claim of improved quality of life for patients with malignant ascites. This is chiefly due to the avoidance of inconvenient hospital stays and improved control of the symptoms of ascites. The proportion of patients who could potentially benefit from PleurX drain placement is inconclusive and there is substantial uncertainty surrounding the proportion of inpatient versus outpatient LVP procedures undertaken currently in the UK. Finally, introduction of PleurX drainage of malignant ascites in the community would require a transfer of financial burden between secondary and primary care budgets which may be a barrier to implementation.
4. National Institute for Health and Clinical Excellence (NICE) guidance

4.1. Preliminary guidance

NICE’s Medical Technologies Advisory Committee considered evidence from several sources: the Sponsor’s submission, EAC report, as well as testimony from experts and one patient with experience of malignant ascites. The Committee decided that:

- “the case for adopting the PleurX peritoneal catheter drainage system in the NHS is supported by the evidence. The available clinical evidence suggests that the PleurX peritoneal catheter drainage system is clinically effective, has a low complication rate and has the potential to improve quality of life.
- The PleurX peritoneal catheter drainage system should be considered for use in patients with treatment-resistant, recurrent malignant ascites.
- The PleurX peritoneal catheter drainage system is associated with an estimated cost saving of £679 per patient when compared with inpatient large-volume paracentesis” (21).

The patient testimony further persuaded the Committee of the burdensome nature of repeated LVP procedures (whether as inpatient or day case), and the huge benefits presented by PleurX through early and frequent removal of ascitic fluid. The Committee acknowledged that patients may often wait for fluid accumulation to reach high levels before arranging to attend hospital for an LVP meanwhile having to tolerate the negative symptoms of malignant ascites. There was debate about the most appropriate point in the pathway for patients with treatment-resistant, recurrent malignant ascites to be treated with PleurX. To define the ascites as recurrent the fluid would need to reaccumulate after several LVP procedures; the Committee decided that the decision to start treatment with PleurX should be shared between clinicians and patients.

Whilst reviewing the cost evidence the clinical experts advised the Committee that the cost of nursing staff may have been overestimated in the PleurX arm of the model because most patients with malignant ascites would receive community nurse visits regardless of whether they have a PleurX drain. In addition, the Committee noted that the cost of a bed day had been underestimated which undervalued the saving attributable to PleurX. Expert opinion was also provided which suggested that day case LVP would be more costly than a PleurX drain, although this was not demonstrated in the Sponsor’s de novo cost model.
4.2. Public consultation

Responses in the public consultation to NICE’s provisional recommendations were broadly positive, and required only one addition to the guidance document. This related to uncertainty surrounding the term “treatment-resistant” to describe the target disease, and one stakeholder requested clarification. It was agreed that the following paragraph should be added:

“The Committee was advised that the term 'treatment-resistant' is normally understood by clinicians to mean that there is a low likelihood of further medical or oncological interventions (particularly chemotherapy) being successful in preventing or reducing re-accumulation of ascites.”

4.3. Final guidance

NICE published the ninth Medical Technologies Guidance (MTG9) on the PleurX peritoneal catheter drainage system for vacuum-assisted drainage of treatment-resistant, recurrent malignant ascites in March 2012 (22). The stakeholder comment was addressed and the provisional guidance remained mostly unchanged.

5. Key Challenges and Learning Points

The EAC recognised several important challenges in reviewing the evidence base for PleurX. These highlight the differences between device and drug evaluations and the difficulties in end-of-life research:

**Challenges of device evaluations compared to those of drugs.** Adoption of innovative medical devices often requires changes in the delivery of patient care in order to be implemented successfully (23). This can impact significantly on any potential cost savings when assessing economic costs against standard UK practice (the comparator). This is rarely the case for drugs where prescribing practice and costs are not so heavily influenced by organisational context. In the case of the comparison between PleurX and LVP, transfer of treatment from secondary care to the community setting drives the PleurX-associated savings. However, variability in UK clinical practice for the treatment of malignant ascites resulted in uncertainty surrounding the cost savings from the release of bed days. Adequate consideration for the wider economic implications of implementing a new technology is often a challenge.

**There was a lack of randomised controlled trials and absence of studies which sit high in the hierarchy of evidence.** The regulatory requirements to bring a medical device to market differ from those of pharmaceuticals and often translate into a lower burden of evidence demonstrating effectiveness of devices (23). The practical, ethical and methodological difficulties in recruiting
patients to end-of-life research means that evaluating a palliative management device like PleurX will rely heavily on observational studies.

**Qualitative studies and patient-reported outcome are essential in malignant ascites research.** Patient-centred outcomes were described in just two studies (13;19). Arguably the most important outcome for terminally ill patients with recurrent, treatment-resistant malignant ascites is improvement in quality of life. This point was eloquently supported by a patient representative at MTAC with experience of the drawbacks of undergoing repeated LVPs. More high quality, qualitative publications and validated patient reported outcome measures are needed to strengthen the evidence base.

(Word count: 3,754 excluding tables)
### Table I – Summary of selected studies and outcomes included in the clinical evidence submission

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Procedural success (no. of procedures)</th>
<th>Catheter patency[^2]</th>
<th>Mean duration of catheter survival (range)</th>
<th>Overall complication rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosenberg 2004 (16)</td>
<td>Retrospective case series; comparative; single centre (USA)</td>
<td>100% (40)</td>
<td>27/40 (67.5%) (11 pts lost to follow up)</td>
<td>NR</td>
<td>3/40 (7.5%) Only failures reported</td>
</tr>
<tr>
<td>Courtney 2008 (13)</td>
<td>Prospective case series; non-comparative; 4 centres (USA)</td>
<td>100% (34)</td>
<td>29/34 (85%) (5 pts lost to follow up)</td>
<td>86 days (lower 95% CI of product limit analysis)</td>
<td>20/34 (59%)</td>
</tr>
<tr>
<td>Mullan 2011 (10)</td>
<td>Pre-publication; retrospective case series; non-comparative; single centre (UK)</td>
<td>100% (52)</td>
<td>50/52% (96%)</td>
<td>59.4 days (4-216 days) does not include failed catheters</td>
<td>8/50 (16%)</td>
</tr>
<tr>
<td>Richard 2001 (15)</td>
<td>Retrospective case series; non-comparative; single centre (USA)</td>
<td>100% (10)</td>
<td>8/10 (80%)</td>
<td>70 days (1-100 days)</td>
<td>2/10 (20%)</td>
</tr>
<tr>
<td>Tapping 2011 (18)</td>
<td>Retrospective case series; non-comparative; single centre (UK)</td>
<td>100% (32)</td>
<td>24/28 (86%)</td>
<td>113 days (5-365 days)</td>
<td>12/28 (43%)</td>
</tr>
<tr>
<td>Saiz-Mendiguren 2010</td>
<td>Retrospective case series; non-comparative; single centre (Spain)</td>
<td>100% (10)</td>
<td>9/10 (90%)</td>
<td>52 days (13-113 days)</td>
<td>0/10 (0%)</td>
</tr>
<tr>
<td>Day 2011 (19)</td>
<td>Poster; qualitative case series; PleurX and LVP patients interviewed; 3 centre (UK)</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Brooks 2006 (12)</td>
<td>Case report, single centre (USA)</td>
<td>N/A</td>
<td>N/A</td>
<td>18 months</td>
<td>3 in 1 patient</td>
</tr>
<tr>
<td>Iyengar 2002 (14)</td>
<td>Case report, single centre (USA)</td>
<td>N/A</td>
<td>N/A</td>
<td>6-12 weeks</td>
<td>1 in 3 patients</td>
</tr>
<tr>
<td>Mullan 2011 (11)</td>
<td>Patients are subset of Mullan et al. (10) full study as Ref: 10</td>
<td>N/A</td>
<td>N/A</td>
<td>NR</td>
<td>N/A</td>
</tr>
</tbody>
</table>

[^2]: Defined as the number of catheters functioning at death, study end point, or resolution of ascites

NR: Not Reported; Not Applicable;
Table II – Threshold analysis of key drivers in models comparing PleurX with both inpatient and outpatient large volume paracentesis.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>PleurX vs Inpatient LVP</th>
<th>PleurX vs Outpatient LVP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost of a hospital bed day (2009-10 value)</td>
<td>£312</td>
<td>£312</td>
</tr>
<tr>
<td>Number of bed days per LVP session (10)</td>
<td>2.8</td>
<td>&lt; 2.1</td>
</tr>
<tr>
<td>Frequency of LVP per month (10)</td>
<td>1.22</td>
<td>&lt; 0.82</td>
</tr>
<tr>
<td>Number of bed days for PleurX catheter placement (10)</td>
<td>1.0</td>
<td>&gt; 3.1</td>
</tr>
<tr>
<td>Cost per drainage kit box (10 units) (2011 values)</td>
<td>£637.50</td>
<td>&gt; £915</td>
</tr>
<tr>
<td>Number of drainage kits used per week per patient (13;15)</td>
<td>3.5</td>
<td>&gt; 5.1</td>
</tr>
</tbody>
</table>
Reference List


