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

A Details of assessment report:

- White J, Carolan-Rees G, Dale M (2011). External assessment centre report: PleurX indwelling peritoneal catheter for vacuum assisted drainage of recurrent malignant ascites at home. September 2011.

B Submissions from the following sponsors:

- UK Medical Ltd.

C References

Ayantunde A and Parsons S (2006) Pattern and prognostic factors in patients with malignant ascites: a retrospective study. Annals of Oncology 18: 945–949

Becker G, Galandi D, Blum HE (2006) Malignant ascites: Systematic review and guideline for treatment. European journal of cancer 42: 589–597.

Courtney A, Nemcek J, Rosenberg S et al. (2008) Prospective evaluation of the PleurX catheter when used to treat recurrent ascites associated with malignancy. Journal of Vascular and Interventional Radiology. 19 (12): 1723–1731.

Day R, Keen A, Perkins P (2011). What are the experiences of patients with malignant abdominal ascites ? [abstract]. In: 12th Congress of the European Association for Palliative Care, May 2011, Lisbon, Portugal.

[redacted]

Iyengar TD, Herzog TJ (2002) Management of symptomatic ascites in recurrent ovarian cancer patients using an intra-abdominal semi-permanent catheter. American Journal of Hospice & Palliative Medicine 19 (1): 35–38.

Mullan D, Laasch H-U, Jacob A et al. (2011a). Tunnelled intra-peritoneal catheters in the management of malignant ascites: Complications and cost implications. In press (manuscript submitted to Journal of Cardiovascular and Interventional Radiology).

Mullan D, Laasch H-U, Jacob A et al. (2011b). Fibrinolysis in the management of malignant ascites and non-functioning intra-peritoneal tunnelled catheters In press (manuscript submitted to Journal of Cardiovascular and Interventional Radiology).

Richard HMI, Coldwell DM, Boyd-Kranis RL et al. (2001) PleurX tunnelled catheter in the management of malignant ascites. Journal of Vascular & Interventional Radiology 12 (3): 373–375.

Rosenberg S, Courtney A, Nemcek AA Jr et al. (2004) Comparison of percutaneous management techniques for recurrent malignant ascites. Journal of Vascular & Interventional Radiology 15 (10): 1129–1131.

Saiz-Mendiguren R, Gomez-Ayechu M, Noguera JJ et al. (2010) Permanent tunneled drainage for malignant ascites: initial experience with the PleurX catheter. Radiologia. 52: 541–45.

Tapping CR, Ling L, Razack A (2011) PleurX drain use in the management of malignant ascites-safety, complications, long term patency and factors predictive of success. CardioVascular and Interventional Radiology. 34:S4.

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.

Dr. Robert Jones

Consultant Interventional Radiologist, British Society of Interventional Radiology

Dr. Hans-Ulrich Laasch

Consultant Interventional Radiologist, British Society of Interventional Radiology

Mrs D A Fitzgerald

Gynaecological Oncology Clinical Nurse Specialist, National Forum of Gynaecology Oncology Nurses

Ms. Lisa Peck

Gynaecological Cancer Nurse, National Forum of Gynaecology Oncology Nurses

- All four experts have been directly involved with the use of this technology. Three of them found it to be a significant modification of the existing technology, and one expert considered it to be a thoroughly novel technology.
- The experts commented that the 'tunnelled' nature of the PleurX catheter allows patients to undergo regular drainage in the community setting and therefore would reduce the need for hospital-based large-volume paracentesis. This may improve the quality of life of patients at the terminal stage of life as they would get the opportunity to spend more time at home.

- The frequent drainage of smaller quantities of ascitic fluid may result in better control of symptoms associated with the accumulation of large amounts of ascites.
- The reduction in large-volume paracentesis procedures owing to the routine use of PleurX catheter drainage system could result in decreased outpatient visits and hospital admissions. Therefore the PleurX peritoneal catheter drainage system is potentially cost saving to the NHS.
- The reduction in large-volume paracentesis procedures would reduce the need for repeated needle punctures and the associated infection risk, and would have further patient and system benefits.
- The experts commented that there would be training requirements for the community healthcare staff. UK Medical Ltd (the PleurX distributor in the UK) provides the free training support.

Appendix C: Comments from patient organisations

Advice and information was sought from patient and carer organisations. The following patient and carer organisations responded:

- Target Ovarian Cancer

The organisation commented that the PleurX peritoneal catheter drainage system has the potential to benefit patients without strong support networks, allowing them to avoid hospital visits and admissions at a very distressing time. The PleurX peritoneal catheter drainage system may decrease the symptoms associated with ascitic fluid accumulation such as bloating and psychological distress, particularly among women. It may also reduce the need for potential emergency admissions, potential overnight hospital stays and medical interventions. However some patients may find self-management of ascites a difficult task and may prefer to attend hospital. NICE guidance on this device would be helpful for wider usage of this device.

Appendix D: Additional submission information

National Institute for Health and Clinical Excellence

National Institute for Health and Clinical Excellence

Additional submission information

PleurX indwelling peritoneal catheter for vacuum assisted drainage of recurrent malignant ascites at home

The purpose of this table is to show where the External Assessment Centre relied in their assessment of the topic on information or evidence not included in the original sponsor submission. This is normally where the External Assessment Centre:

- become aware of additional relevant evidence not submitted by the sponsor
- need to check “real world” assumptions with NICE’s Expert Advisers, or
- need to ask the sponsor for additional information or data not included in the original submission

These events are recorded in the table to ensure that all information relevant to the assessment of the topic is made available to MTAC. The table is presented to MTAC in the assessment report overview, and is made available at public consultation.

Submission document section/sub-section number	Question/request to sponsor or expert adviser Please indicate whether manufacturer or expert adviser was contacted. If an expert adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action/ impact/other comments
Literature search strategy (Appendix 2)	In their literature search the manufacturer has searched several associations/conference proceedings as part of their "grey literature search". They are the following: • British Society for Interventional Radiologists (BSIR) • European Association for Palliative Care (EAPC) • Society of Gastrointestinal Intervention (SGI) • British Society of Gastrointestinal and Abdominal Radiology (BSGAR) • British Society of Gastroenterology (BSG) From your experience would these societies encompass the majority of relevant unpublished posters/abstracts/presentations in this area? If not, are there any other key societies/meetings you can point me towards?	**EXPERT 1:** There are no UK cancer specific societies included, I am unaware who they are, but they should be interested. **EXPERT 2:** British Gynaecological Cancer Society National Forum of Gynaecological Oncology Nurses	**Cancer-specific societies were searched for grey literature by EAC**
Section 1.13	A couple of the cited publications on the use of PleurX for palliative treatment of malignant ascites use prophylactic antibiotics during placement of the catheter, others do not use any. Do you have thoughts on whether the use of prophylactic antibiotics is commonplace/ standard treatment / individual to the patient in the NHS?	**EXPERT 1:** We do not use them. It is an antiseptic procedure like a central line insertion and antibiotic prophylaxis is not recommended for these. **EXPERT 2:** Individual to the patient in the NHS – not used here to my knowledge **EXPERT 3:** We do not routinely use prophylactic	**Consensus that prophylactic antibiotics not used in NHS. No**

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		antibiotics during pleurx placement at our hospital. I cannot comment on the use of antibiotics elsewhere within the NHS in this setting. NB:- If there was any sign of infection (locally or systemically) at the proposed time of insertion we would delay pleurx placement. We routinely screen for infection prior to pleurx placement in all cases.	**action required.**
General	Would indwelling drainage catheters such as PleurX be monitored by regular culture of fluid for peritonitis, or would cultures only be tested when there were clinical symptoms in the patient?	**EXPERT 1:** No routine monitoring. Investigations in case of fever or abdominal pain. Fluid may "normally" be blood-stained or murky. **EXPERT 2:** Definitely not regular cultures, only when clinical symptoms which have been very rare indeed. **EXPERT 3**: In our experience cultures would only be obtained if there were clinical symptoms or if there was a change in the colour / consistency of the fluid.	**Consensus that routine culturing of ascitic fluid is not commonplace. No action required.**
Section 2.4	How does PleurX fit into the pathway of care for patients with malignant ascites?	Patients come to us who have are having multiple admissions for LVP procedures. An appointment is made for the PleurX drain to be inserted under radiological guidance. At that point UK Medical is notified and their account managers will contact the district nurse who will be visiting the patient at home. UK Medical then provides training to the district nurse in how to use the PleurX drain.	**General information. Comments support assumptions made in**

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		They will also train the patient. UK Medical has provided an excellent service in this respect. In some cases, if there has been no prior notice to UK Medical before the drain is inserted, the rep will arrange to carry out the training session with the district nurse and patient in the patient's home.	**economic model. No action required.**
General	How easy is the PleurX drain to use? Are district nurses happy to use the system?	Drain is very simple. We have treated many patients and have only had one possible infection. The district nurses are happy to learn how to use the drain, so too are the patients and relatives. Often the nurse will visit during the first couple of weeks and after that point the patient or relative will carry out the drainage session themselves without the need for a district nurse to come. Patients are often very keen to carry out the drainage themselves.	**Checking barriers to adoption of device. No action required.**
Section 2.8	Would these patients be receiving district nurse visits if they were not using the PleurX drain? How many extra visits from a nurse would be needed if the PleurX drain was in situ?	It is very likely that a district nursing team would be involved in providing care at the patients' home to some extent, whether or not the patient had PleurX. The district nurse may provide a few extra visits to begin with (on top of what they normally would) but after a few weeks most patients choose to change the drain bottles themselves. PleurX really requires minimal input from the nursing team, and it is unlikely that a nurse would continue	**Comment included in EAC report. Suggests manufacturer has used a conservative inputs to**

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		to perform the drainage sessions.	**estimate costs of nursing visits (bias against PleurX)**
Section 2.5	Can you use PleurX with multi-loculated ascites?	In our hospital the radiologist would decide on a case-by-case basis. If it can be done, the drain will be inserted into the largest fluid pocket. Sometimes paracentesis is needed to drain smaller pockets.	**Relevant information on potential exclusions for PleurX treatment. No further action taken.**
General	Would you be more likely to give PleurX to a healthy, younger patient?	No. Patients who are active and reasonably well benefit hugely from PleurX. But so do frailer, less well or older patients as it means that they don't have to regularly go into hospital in order to have their ascites drained. The symptoms of ascites can be very debilitating and so keeping the fluid from accumulating to large volumes benefits all patients.	**Relevant information on potential bias in patient selection criteria. No further action required.**

Submission document section/sub-section number	Question/request to sponsor or expert adviser Please indicate whether manufacturer or expert adviser was contacted. If an expert adviser, only include significant correspondence and include clinical area of expertise.	Response Attach additional documents provided in response as Appendices and reference in relevant cells below.	Action/ impact/other comments
Cost of treating complications (Section 6.4.7)	In patients with complications such as peritonitis or occlusion of PleurX due to loculated ascites, would it be standard practice to admit them for treatment? If so, could you give any idea of their inpatient stay?	I suspect admission would be required. If patients were admitted, the length of stay would probably be determined by the individual clinical scenario.	**Comment suggests that cost of complications have been underestimated in model.**
Section 6.4.7	In your hospital how do you manage peritonitis due to PleurX?	We have not encountered this to date. But I suspect this would involve removal of the drain and antibiotics at the very least.	**As above**
General	Could you provide any details of informal or formal criteria used in your hospital to decide whether or not to treat using PleurX. Specifically the following: • Life expectancy • Number / frequency of previous paracentesis • Presence/absence of multi-loculated ascites • Mobility or ability to perform drainage themselves.	**EXPERT 1:** The criteria we use is based on the worldwide evidence and experience. We only carry out pleurx in patients with limited life expectancy and a palliative outlook whom have had at least 3 episodes of recurrent and symptomatic ascites following normal paracentesis over a short period of time. We would not routinely consider pleurx in multi-loculated ascites / effusions. Patient understanding and cooperation is of utmost importance and we educate each potential patient and give them the choice. Individual ability to perform drainage is not necessarily essential but adequate family and community nursing support is. **EXPERT 2:** If the patient has no further chemotherapy	**General information on potential exclusion criteria for treatment with PleurX. Relevant to population size.**

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		options and the ascites recurs within a month a PleurX is considered. We have daycase paracentesis now established as an alternative, giving the patient the option to some extent. However if the patient needs 2 or more drainages per month we would definitely recommend a PleurX. If inpatient paracentesis is the only alternative, we would recommend it for most recurrent ascites. Streptokinase has expanded the use in loculated ascites. Often disruption of the septa with a guidewire does the same job, although the loculation is often incomplete. Drainage is mostly preformed by district nurses, so mobility is not a major issue.	
Section 2.2	Is there a subset of malignant ascites patients whose fluid accumulation resolves after just one or two paracenteses? And therefore PleurX may not be suitable/necessary. If so, could you give an idea of proportion?	**EXPERT 1:** I cannot comment on this with accuracy. But we only consider pleurx after 3 paracenteses. **EXPERT 2:** This only really happens if the patient has further treatment, reducing the tumour in the abdomen (again an oncology opinion would be helpful). If further treatment is available we withhold a PleurX. However we do not insert a PleurX de novo - so we always ahve a baseline interval for the recurrence.	**General information on population estimate. No action required.**
Section 6.4.7	Several papers have used multi-loculated ascites as an exclusion criterion for treatment with PleurX. How would a loculations be visualised/diagnosed before catheter insertion?	Loculations are best assessed with ultrasound prior to considering pleurx insertion. I do think this is an appropriate exclusion criteria although the number and size of loculations should be considered.	**Information on exclusion criteria for**

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	Do you think that this is an appropriate exclusion criteria? If so, how are these patients treated? How prevalent are loculations amongst patients with malignant ascites?	Large locules could be targeted with conventional drains.	**treatment with PleurX. Included in report.**
Section 2.4	The insertion procedure guidance technique varies across studies with US, fluoroscopy, and CT (or a combination) being used for catheter insertion. What are the considerations for choice of guidance technique?	In our experience we use ultrasound for pleurx placement in malignant ascites without fluoroscopy and a combination of both for placement in pleural effusions.	**Information on treatment pathway. Comment included in report.**
Section 2.4	Some publications use local anaesthetic alone, others use conscious sedation with LA. Is this simply a matter of patient preference? Would sedation always be offered?	We use local anaesthetic in all cases. The use of sedation is then considered on a case by case basis but is always offered.	**Information on treatment pathway. Comment included in report.**
Economic model general	How common is it to perform conventional LVP in the outpatient setting?	I would say this varies from centre to centre and patient condition.	**Information on predominance of inpatient**

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information			**versus outpatient LVP. No action taken.**
Section 2.7	If treating patients with conventional LVP how would you manage loculated ascites? Are fibrinolytics used?	By targeting large locules. I have not had any experience with the use of fibrinolytics in this setting so unable to comment.	**No action taken.**

Appendix E: Sponsor's factual check of the assessment report and the External Assessment Centre's responses

The following table presents the issues raised by the sponsor in relation to the EAC report, and the EAC's response to each of these comments. Any actions taken by the EAC to address the issues have been explained.

Issue 1

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Response
UK Medical is referred to as 'The Manufacturer' throughout the document.	UK Medical should be referred to as 'The Sponsor'	The manufacturer of the Pleurx peritoneal drainage system is CareFusion	Amendment accepted.

Issue 2

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Response
Page 14 highlights 4 bullet points surrounding aspects of the care pathway which require elaboration.	These areas are addressed in the Pleurx peritoneal catheter mini kit 'Instructions for Use'.	IFU's are available upon request and available online	Amendment accepted. Section 2.2 of the EAC report has been changed to reflect the information available in the IFU.

Issue 3

Description of factual inaccuracy	Description of proposed amendment	Justification for amendment	EAC Response
Page 6 states “In this second submission the clinical evidence was substantially updated to include additional material identified by the EAC which was not previously agreed or anticpated.”	We propose “which was not previously agreed or anticipated” be omitted from this sentence.	UK Medical understood that following the initial submission report on the 22nd July it would be acceptable to include additional unpublished material and non-English data for the subsequent submission on 19th August.	Amendment accepted.