NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

Review Decision

Review of MTG9: The PleurX peritoneal catheter drainage system for vacuum-assisted drainage of treatment-resistant, recurrent malignant ascites

This guidance was issued in March 2012 and reviewed in October 2017.

NICE proposes an amendment of published guidance if there are no changes to the technology, clinical environment or evidence base which are likely to result in a change to the recommendations. However the recommendations may need revision to correct any inaccuracies or to update to current formats. The decision to consult on an amendment of published guidance depends on the impact of the proposed amendments and on NICE's perception of their likely acceptance with stakeholders. NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance.

1. Recommendation

Amend the guidance to reflect changes in the technology name from PleurX to PeritX and the new costs. The factual changes proposed have no material effect on the recommendations.

Update the format of the recommendations and insert a section below section 1 titled 'Why the committee made these recommendations', in line with the current template wording and presentation.

Do not consult on the review proposal.

Please see Appendix 1 for a list of the options and their explanations for consideration.

2. Original objective of guidance

To assess the case for adoption of PleurX for vacuum-assisted drainage of treatment-resistant, recurrent malignant peritoneal ascites.

3. Current guidance

1.1 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: it enables early and frequent treatment of symptoms of ascites, in the community, rather than waiting for inpatient treatment.

1.2 The PleurX peritoneal catheter drainage system should be considered for use in patients with treatment-resistant, recurrent malignant ascites.

1.3 The PleurX peritoneal catheter drainage system is associated with an estimated cost saving of £1,051 per patient when compared with inpatient large-volume paracentesis [2018].

4. Rationale

The company has changed the technology's name to PeritX in order to achieve consistency with the intended use (peritoneal fluid drainage). However, there have been no functional changes to the technology.

There is new clinical evidence since the first guidance review. The NICE technical team reviewed this evidence and concluded that it is consistent with the recommendations in MTG9.

For the cost case, the original cost model was updated to current prices for PleurX, comparators and other relevant economic parameters. The 2022 cost update found that PleurX remains cost-saving compared to inpatient large volume paracentesis (LVP) and the savings have increased relative to those in the 2017 cost update. The technology was found to remain cost incurring compared to outpatient LVP. The committee originally considered the case for adoption for PleurX was supported on the basis of the cost savings compared with inpatient LVP. The EAC in the original guidance and in the 2022 cost update found there is a lack of evidence about the proportion of patients treated using LVP in an inpatient versus outpatient setting. In the 2022 update it heard expert opinion that there may be a trend toward the procedure being performed more in an outpatient setting, but that it is not established practice in the NHS. The conclusions in the guidance are thus considered to remain the same. NICE therefore considers the changes have no material effect on the recommendations, and recommends that the guidance is only amended to reflect cost changes, as well as changes to the technology name and updates to current recommendation format/style.

5. New evidence

The search strategy from the original assessment report was re-run. References from October 2017 onwards were reviewed. Additional searches of clinical trials

registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the care pathways. The company was asked to submit all new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked indication for use for their technology. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

5.1 Technology availability and changes

The company has changed the technology's name to PeritX in order to achieve consistency with the intended use (peritoneal fluid drainage). The cost of the technology has increased from £245 to £257.25 and from £64 to £66.94 for the catheter kit and vacuum bottle respectively.

5.2 Clinical practice

There are no NICE guidelines that explicitly describe the care pathway for the management of malignant ascites. NICE guideline NG142 End of life care for adults: service delivery (particularly recommendation 1.2) is concerned with holistically assessing end of life needs.

Two experts contributed to this review and both stated that the care pathway for malignant ascites has not changed since the time of the original guidance. The comparator procedure in the UK is the same and consists of LVP. There remains no clear standard practice for the setting in which LVP is performed in the NHS, which could be as an inpatient, outpatient or day case procedure.

5.3 NICE facilitated research

None.

5.4 New studies

The company did not submit any studies in response to NICE's request for clinical evidence published after the first guidance review. NICE information services repeated the original search strategy from MTG9 with revised dates (October 2017 to February 2022). Review articles and full papers and abstracts that did not mention the technology used were excluded. 8 relevant studies were identified and are summarised below, including 1 prospective study, 3 retrospective studies, 1 case report and 3 abstracts. The abstracts do not concern PleurX, but describe current advances in the management of ascites with paracentesis. The cost of paracentesis and the assumption that it

happens in an inpatient setting are key cost drivers in the economic model (see section 5.5).

Petzold et al. 2021

A prospective study comparing the safety and efficacy of PleurX and LVP in patients with symptomatic, diuretics-refractory ascites in University Medical Center Goettingen, Germany. The sample size was 51 patients (64.7% male). Patients had a mean of 2.20 (±1.67) LVP procedures before PleurX placement (range 0–7 procedures). Outcomes included number of catheter days, complications, amount of drained ascites and ascites-associated symptoms and hospitalization rate pre- and post-PleurX insertion. Correlation was assessed, but the results were not adjusted for patient characteristics, e.g. pharmacological treatment (received by 22 of the patients) or type of cancer.

Key findings:

- The technical success rate of PleurX implantation was 100%.
- 85.7% of assessed patients reported an improved general condition 30 days after PleurX insertion. This is based on 17 patients for whom symptoms could be assessed at this time point.
- Abdominal discomfort, impaired mobility, dyspnoea, fatigue, nausea and vomiting were significantly reduced 30 days after PleurX insertion ($p<0.05$, n=17). The symptoms were also reduced at 3 months after insertion ($p=0.06$, n=6).
- Major complications were cellulitis (n=2), peritonitis (n=1) and drainage dislocation (n=1). For those cases, the catheter had to be explanted.
- The mean hospitalization rate within 30 days or until death, respectively, was 11.27% (±21.59) compared to 27.08% (±18.36) before implantation ($p<0.001$).

Korpi et al. 2018

A retrospective comparative study investigating success of drainage, complications, and survival after paracentesis or PleurX in patients with malignant ascites in Tampere University Hospital in Finland. Importantly, both paracentesis and catheter insertion were done in an outpatient setting. The sample size was 104 patients (44% male) who underwent 118 paracenteses and 48 PleurX insertions. Outcomes included success and volume of ascites drainage, complication rates, and survival after PleurX procedure in days. Cox proportional hazard regression analyses were used to evaluate the influence of procedure type, volume of removed ascites fluid, cancer type, and whether

chemotherapy was ongoing, on age-adjusted survival time after the procedure.

Key findings:

- Drainage of ascites fluid was successful in all cases, including with outpatient paracentesis (currently not standard care in the NHS). Median ascites volume was 3700 mL (range 300–13,200 mL).
- Complication rates were 7% and 25% for paracenteses and PleurX, respectively. Most of the complications were minor. Repeated procedures were significantly less for PleurX (64% versus 10%, $p<0.001$). Two PleurX patient were admitted to the hospital for a period of greater than one day due to complications. There were no deaths directly associated with the catheter.
- Median survival after the first procedure was 40 days (interquartile range 17–115). The volume of removed ascites fluid or procedure type were not associated with survival. Pancreatic cancer was associated with shorter median survival whereas receiving chemotherapy with longer median survival.
- The authors suggested that paracentesis may be a better solution for people with a very short survival time (<1 month) such as pancreatic cancer patients, if risk stratification can be done accurately. They note as a reason that based on previous research, LVP has to be repeated in 64% of the cases in a median of 14 days.

Knight et al. 2018

A retrospective non-comparative study carried out by the Mayo Clinic, Massachusetts, USA, investigating the safety and efficacy of PleurX in patients with malignant and non-malignant ascites. The sample size was 137 patients (56% male) of which 119 (87%) underwent PleurX insertion for malignant ascites. Outcomes included number of prior paracenteses, success and volume of ascites drainage at time of insertion, complication rates, reason for complication, and catheter dwell time prior to infection in days.

Key findings:

- The median number of prior paracenteses was 3 (range 1–38). It was significantly greater in patients with non-malignant versus malignant ascites (median, 11 versus 2, $p<0.0001$). This finding is expected, as survival time was not adjusted for and people with malignant ascites will likely have a shorter median survival resulting in fewer interventions.

- The technical success rate of PleurX implantation was 100%. The mean (± SD) volume of ascites drained at the time of procedure was 2.5 ± 1.4 L.
- Nineteen patients (13.9%) experienced a total of 11 minor and 12 major complications. Nine patients developed a catheter-associated infection. The remaining complications included leakage at the dermatotomy site (n=8), catheter dislodgement (n=2), obstruction (n=2), and groin pain (n=2). There was one catheter-associated death from bacterial peritonitis. Twelve indwelling catheters were removed before the patients' death.
- Patients who developed a catheter-associated infection had a significantly longer catheter dwell time compared to those who did not develop an infection (median 96.5 versus 20 days, respectively; $p<0.01$). This is a common finding across all types of indwelling catheters.

Gupta et al. 2020a

A retrospective non-comparative study evaluating the incidence, risk factors and management of hyponatremia (low blood sodium levels) after indwelling peritoneal catheter (IPC) placement in a tertiary care hospital in the USA. Confusion, hyponatremia, and, in severe cases, hypotension and acute kidney injury are signs and symptoms of severe depletion in patients who undergo aggressive drainage. The study sample size was 309 patients (39% male). It is unclear how many underwent PleurX insertion and how many insertions were for malignant ascites management. The same team published a case series of 3 patients with PleurX, hospitalised between 2017 and 2019 due to "PleurX desalination" (Gupta et al. 2020b). Outcomes in the Gupta et al. 2020a study included incidence of hyponatremia (with a serum sodium level <135 mEq/L) after IPC placement, the risk factors for its development, and how it was managed.

Key findings:

- The incidence of hyponatremia after IPC placement was 84.8% (n=262) of whom 21 patients (8.0%) had severe hyponatremia.
- Patients with prior hyponatremia had 8-fold odds of having persistent hyponatremia after IPC placement (odds ratio, 7.9; 95% CI, 2.9-21.7). Patients with hepatopancreatobiliary neoplasms were more likely to develop hyponatremia (29.8% versus 14.9%).
- Hyponatremia was either unrecognized or untreated in 189 patients (72.1%).
- The authors concluded that people at highest risk of hyponatremia, such as those with hyponatremia at baseline and those with

hepatopancreatobiliary neoplasms, should be evaluated carefully prior to IPC placement and may warrant closer monitoring after placement.

Hacking et al. 2020

A case report describing the first case of a patient with two PleurX indwelling catheters. The case is from the UK. Insertion of the second catheter was necessary as the position of the first was inadequate for further fluid removal, following an increase in size of the cystic mass posterior to the stomach. The patient had a very rare form of mesenchymal cell cancer, namely gastrointestinal stromal tumour. The incidence in the UK is 900 per annum.

Lee 2021

A report of a hospital that introduced an advanced practice nurse-led ambulatory abdominal paracentesis service along inpatient procedures in response to high hospital bed occupancy during the COVID-19 pandemic. A multidisciplinary team developed workflows and safety guidelines. Data was gathered over 11 months and length-of-stay (LOS) and adverse events were tracked. There was a significant reduction in average LOS (1.48 versus 5.82 days, $p<0.001$). 86.8% of paracenteses were performed in one day, with the remainder over 2 days. The day unit service encountered only 10 adverse events requiring admission to the ward for continued drainage. This study is in abstract form only.

Doran et al. 2016

This study reports on a quality improvement project looking at time to paracentesis in patients admitted to Truman Medical Center, USA. The aim of the study was to reduce time to paracentesis since delayed paracentesis is associated with a 2.7-fold increased risk of mortality. It is not clear what the actual intervention involved, but the centre managed to improve the percentage of paracenteses within 12 hours from 19% to 36%. The study sample size is very small (n=11) and the study is in abstract form only.

Willmann et al. 2019

This retrospective study reports on an elective paracentesis programme in an outpatient setting over 3 years. The procedure was performed by junior medical officers on 66 patients. Most ascites were due to liver disease. The rate of spontaneous bacterial peritonitis was 5.5%, higher than reported rates of 1.5-3.5%. Adherence to guidelines for utilization of secondary spontaneous bacterial peritonitis prophylaxis was suboptimal. This study is in abstract form only.

5.5 Cost update

King's Technology Evaluation Centre (EAC) was commissioned to review and update the PleurX cost case (see the EAC costing update report). It considered that the model structure remained valid because there was no change in the clinical pathway since the first guidance review. All costs in the model were updated to current prices. The cost model compared PleurX to both inpatient and outpatient LVP, however the EAC kept the assumption that LVP is largely provided in an inpatient setting (at the time of the original guidance, the committee were advised that many people may not prefer LVP in an outpatient setting compared to inpatient, and no further data on the proportion of people treated with LVP in each setting became available by the time of the review). The results of the analysis suggest that compared to inpatient LVP, the cost savings have increased by £44 from the 2018 update, from £1,051 to £1,095 per patient. However, compared to outpatient LVP, the technology is still cost-incurring, with a cost rise of £25 (from -£871 to -£896 per patient). One of the experts stated that the technology remains "a hugely cost-effective system compared to conventional inpatient paracentesis with massive benefits to the patients and their independence".

6. Summary of new information and implications for review

The new clinical evidence is consistent with the recommendations in the original guidance. The internal team concluded that all new evidence reported favourable outcomes associated with using PleurX. The updated cost modelling shows that PleurX compared to inpatient LVP remains cost saving. Although the technology is cost incurring compared to outpatient LVP, the EAC felt that the procedure performed in an outpatient setting is not established practice in the NHS, based on expert opinion. The recommendations in MTG9 acknowledge this. The internal team has advised that based on its review, the recommendations in MTG9 do not need to be changed.

7. Implications for other guidance producing programmes

No comments for implications for other guidance producing programmes were received during the internal consultation stage. NICE's Interventional Procedures programme is currently working on IPG10194 Tunnelled peritoneal drainage catheter insertion for refractory ascites in cirrhosis, which investigates the technology as one of several options, but this is a different population compared to the scope of this review topic.

8. Implementation

The company provided a list of 37 hospitals where PleurX is used. One of the experts during the review stated that a different drain is mainly used in their practice due to cost considerations.

9. Equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

People with cancer are covered by equalities legislation under the protected characteristic of disability. The PleurX peritoneal catheter drainage system may enable people to have independent control of their symptoms and fit treatment around their normal lives and so to promote equality of opportunity. During original guidance development the Committee considered that the PleurX peritoneal catheter drainage system may have the potential to improve the quality of life for such people and, therefore, promote equality.

No new equality considerations were identified.

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Appendix 1 – Explanation of options

If the published Medical Technologies Guidance needs updating NICE must select one of the options in the table below:

Options	**Consequences**	**Selected – 'Yes/No'**
Amend the guidance and consult on the review proposal	The guidance is amended but the factual changes proposed have no material effect on the recommendations.	No
Amend the guidance and do not consult on the review proposal	The guidance is amended but the factual changes proposed have no material effect on the recommendations.	Yes

Standard update of the guidance	A standard update of the Medical Technologies Guidance will be planned into NICE's work programme.	No
Update of the guidance within another piece of NICE guidance	The guidance is updated according to the processes and timetable of that programme.	No

If the published Medical Technologies Guidance does not need updating NICE must select one of the options in the table below:

Options	**Consequences**	**Selected – 'Yes/No'**
Transfer the guidance to the 'static guidance list'	The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Medical Technologies Guidance on the static list should be flagged for review.	N/A
Defer the decision to review the guidance	NICE will reconsider whether a review is necessary at the specified date.	N/A
Withdraw the guidance	The Medical Technologies Guidance is no longer valid and is withdrawn.	N/A

Appendix 2 – Supporting information

Relevant NICE work

Published

NICE guideline NG12 Suspected cancer: recognition and referral (2015, updated 2021)

NICE clinical guideline CG122 Ovarian cancer: recognition and initial management (2011)

NICE clinical guideline CG104 Metastatic malignant disease of unknown primary origin in adults: diagnosis and management (2010)

NICE interventional procedures guidance on Tunnelled peritoneal drainage catheter insertion for treatment-resistant, recurrent ascites due to cirrhosis. Expected publication date: November 2022.

Registered and unpublished trials

Trial name and registration number	Details
None	-

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Appendix 3 – Changes to guidance

Table 3: Proposed amendments to original guidance

Section of MTG	Original MTG	Proposed amendment
Overview	In February 2018, this guidance was updated to include a review of the cost model using more recent values. New evidence and updated costs identified during the guidance review are denoted as [2018].	In February 2018, this guidance was updated to include a review of the cost model using more recent values. A second guidance review was done in 2022 which further reviewed new evidence and updated costs, updates for here are denoted as **[2022]**. During this second guidance review, the company indicated that the technology name has been changed from PleurX to PeritX, so this has been changed where relevant.
Page 1	The PleurX peritoneal catheter drainage system for vacuum-assisted drainage of treatment-resistant, recurrent malignant ascites	The PeritX peritoneal catheter drainage system for vacuum-assisted drainage of treatment-resistant, recurrent malignant ascites
Page 4, 1.1	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: it enables early and frequent treatment of symptoms of ascites, in the community, rather than waiting for inpatient treatment.	The PeritX system is recommended as an option for drainage of treatment-resistant, recurrent malignant peritoneal ascites.
Page 4, 1.2	The PleurX peritoneal catheter drainage system should be considered for use in patients with treatment-resistant, recurrent malignant ascites.	[section to be removed]

Page 4, 1.3	The PleurX peritoneal catheter drainage system is associated with an estimated cost saving of £1,051 per patient when compared with inpatient large-volume paracentesis [2018].	[section to be removed]
Why the committee made these recommendations	-	Clinical evidence shows that the PeritX peritoneal catheter drainage system is effective for managing treatment-resistant, recurrent malignant peritoneal ascites. It may improve quality of life for some people with cancer, by enabling early and frequent treatment of symptoms of ascites in the community, rather than waiting for inpatient treatment. The PeritX system can lead to an estimated cost saving of £1,095 per person compared with inpatient large-volume paracentesis.
Page 5, 2.1	The PleurX peritoneal catheter drainage system (BD) is intended for use in the management of treatment-resistant, recurrent malignant ascites (accumulation of fluid in the peritoneal cavity) in the community setting [2018].	The PeritX peritoneal catheter drainage system (BD) is intended for use in the management of treatment-resistant, recurrent malignant ascites (accumulation of fluid in the peritoneal cavity) in the community setting **[2022]**.
Page 5, 2.2	The PleurX peritoneal catheter is made of silicone and is 71 cm in length and 5.12 mm (15.5 Fr) in diameter. The distal end of the catheter has several side holes and is placed in the peritoneal cavity. There is a polyester cuff midway along the catheter, which is sited 1–2 cm within a subcutaneous tunnel and helps to secure the catheter in place by encouraging tissue growth into the polyester. The external end of the PleurX peritoneal	The PeritX peritoneal catheter is made of silicone and is 71 cm in length and 5.12 mm (15.5 Fr) in diameter. The distal end of the catheter has several side holes and is placed in the peritoneal cavity. There is a polyester cuff midway along the catheter, which is sited 1–2 cm within a subcutaneous tunnel and helps to secure the catheter in place by encouraging tissue growth into the polyester. The external end of the PeritX peritoneal

	catheter has a safety valve that prevents air entering or fluid leaking out of the catheter. A cap protects the valve and prevents debris from building up.	catheter has a safety valve that prevents air entering or fluid leaking out of the catheter. A cap protects the valve and prevents debris from building up.
Page 5, 2.3	The drainage system comprises a 1-litre vacuum bottle with a drainage line that connects to the PleurX peritoneal catheter for fluid removal. It also includes a procedure pack that contains the supplies needed to perform the drainage procedure and to replace the cap and the gauze pad dressing over the catheter.	The drainage system comprises a 1-litre vacuum bottle with a drainage line that connects to the PeritX peritoneal catheter for fluid removal. It also includes a procedure pack that contains the supplies needed to perform the drainage procedure and to replace the cap and the gauze pad dressing over the catheter.
Page 5, 2.4	The PleurX peritoneal catheter is designed to remain in place indefinitely and patients and carers are trained to perform fluid drainage when needed by attaching the vacuum bottle to the catheter. A fresh valve cap and dressing are applied once the drainage is completed. For the majority of the time, the catheter is coiled up and covered with a gauze pad and a waterproof dressing.	The PeritX peritoneal catheter is designed to remain in place indefinitely and patients and carers are trained to perform fluid drainage when needed by attaching the vacuum bottle to the catheter. A fresh valve cap and dressing are applied once the drainage is completed. For the majority of the time, the catheter is coiled up and covered with a gauze pad and a waterproof dressing.
Page 5, 2.5	The list prices stated in the sponsor's submission for the PleurX peritoneal catheter and the PleurX drainage kit with a 1-litre vacuum bottle are £245 and £64 per unit respectively.	The list prices stated in the sponsor's submission for the PeritX peritoneal catheter and the PeritX drainage kit with a 1-litre vacuum bottle are £245 and £64 per unit respectively. The updated costs are £257.25 and £66.94 respectively **[2022]**.
Page 5, 2.6	The claimed benefits of the PleurX peritoneal catheter drainage system in the case for adoption presented by the sponsor are: • Repeated drainage of ascitic fluid in community settings	The claimed benefits of the PeritX peritoneal catheter drainage system in the case for adoption presented by the sponsor are: • Repeated drainage of ascitic fluid in community settings

	may allow greater patient independence, and the flexibility to fit the drainage procedure into their daily lives. • Better symptom control by frequent drainage of smaller quantities of ascitic fluid. Symptoms associated with the accumulation of large amounts of ascites include breathlessness, nausea, bloating, acid reflux, abdominal pain, early satiety, reduced mobility and psychological distress related to negative body image. • Reduced need for repeated large-volume paracentesis procedures and the associated risk of infection from repeated catheter insertion. • Resource savings through a reduced need for hospital physician and nurse time, outpatient visits and hospital bed days.	may allow greater patient independence, and the flexibility to fit the drainage procedure into their daily lives. • Better symptom control by frequent drainage of smaller quantities of ascitic fluid. Symptoms associated with the accumulation of large amounts of ascites include breathlessness, nausea, bloating, acid reflux, abdominal pain, early satiety, reduced mobility and psychological distress related to negative body image. • Reduced need for repeated large-volume paracentesis procedures and the associated risk of infection from repeated catheter insertion. • Resource savings through a reduced need for hospital physician and nurse time, outpatient visits and hospital bed days.
Page 4, 3.1	The key clinical outcomes for the PleurX peritoneal catheter drainage system presented in the decision problem were: • technical success of catheter insertion and drainage procedure	*(NB – PeritX referred to as PleurX in this summary of clinical evidence, as this was the name of the device at the time this evidence was compiled).*The key clinical outcomes for the PleurX peritoneal catheter drainage system presented in the decision problem were:

	• resolution of symptoms (bloating, nausea, acid reflux, reduced appetite, negative perception of body image and resulting psychological distress) • quality of life outcomes • adverse events (catheter site infections, peritonitis, catheter occlusion, and haemorrhage or bowel perforation when the device is inserted) • drainage frequency • resource use outcomes, for example re-admission rates, re-interventions and duration of hospital stay.	• technical success of catheter insertion and drainage procedure • resolution of symptoms (bloating, nausea, acid reflux, reduced appetite, negative perception of body image and resulting psychological distress) • quality of life outcomes • adverse events (catheter site infections, peritonitis, catheter occlusion, and haemorrhage or bowel perforation when the device is inserted) • drainage frequency resource use outcomes, for example re-admission rates, re-interventions and duration of hospital stay.
Page 10, 3.11	The committee concluded from the available clinical evidence that the PleurX peritoneal catheter drainage system is effective in the palliative management of treatment-resistant, recurrent malignant ascites. It has a high procedural success rate, a low complication rate and the potential to improve patient quality of life.	The committee concluded from the available clinical evidence that the PeritX peritoneal catheter drainage system is effective in the palliative management of treatment-resistant, recurrent malignant ascites. It has a high procedural success rate, a low complication rate and the potential to improve patient quality of life.
Page 11, 3.12	Patients with malignant ascites have a disability as defined by the Equality Act 2010. The committee recognised that treatment-resistant, recurrent malignant ascites often has an adverse impact on patients' activities of daily	Patients with malignant ascites have a disability as defined by the Equality Act 2010. The committee recognised that treatment-resistant, recurrent malignant ascites often has an adverse impact on patients' activities of daily living, which may be

	living, which may be improved with the PleurX peritoneal catheter drainage system. The committee was advised by the patient and clinical experts that improvement in quality of life is mainly a result of avoiding regular hospital visits and inpatient stays associated with large-volume paracentesis, and alleviation of symptoms associated with massive ascites through the frequent drainage of small volumes of ascitic fluid.	improved with the PeritX peritoneal catheter drainage system. The committee was advised by the patient and clinical experts that improvement in quality of life is mainly a result of avoiding regular hospital visits and inpatient stays associated with large-volume paracentesis, and alleviation of symptoms associated with massive ascites through the frequent drainage of small volumes of ascitic fluid.
Page 11, 3.13	The committee recognised the uncertainty about the point in the care pathway at which it would be clinically appropriate to treat patients with treatment-resistant, recurrent malignant ascites with the PleurX peritoneal catheter drainage system. Tapping et al. (2011) considered that patients who had had at least 3 previous large-volume paracentesis procedures would be suitable for treatment with the PleurX peritoneal catheter drainage system, whereas Courtney et al. (2008) inserted the PleurX peritoneal catheter in patients who had had at least 2 large-volume paracentesis procedures in the previous 30 days. The committee considered that the decision to start treatment with the PleurX peritoneal catheter drainage system should be shared between clinicians and patients.	The committee recognised the uncertainty about the point in the care pathway at which it would be clinically appropriate to treat patients with treatment-resistant, recurrent malignant ascites with the PeritX peritoneal catheter drainage system. Tapping et al. (2011) considered that patients who had had at least 3 previous large-volume paracentesis procedures would be suitable for treatment with the PeritX peritoneal catheter drainage system, whereas Courtney et al. (2008) inserted the PeritX peritoneal catheter in patients who had had at least 2 large-volume paracentesis procedures in the previous 30 days. The committee considered that the decision to start treatment with the PeritX peritoneal catheter drainage system should be shared between clinicians and patients.
Page 11, 3.15	The committee acknowledged that the current evidence is based on observational studies, with very limited data available comparing the PleurX	The committee acknowledged that the current evidence is based on observational studies, with very limited data available comparing the PeritX

	peritoneal catheter drainage system with other treatments.	peritoneal catheter drainage system with other treatments.
Page 11, 3.16	The committee noted that there are 2 ongoing clinical trials using the PleurX peritoneal catheter drainage system. One is investigating the impact on quality of life and the other is comparing early stage PleurX peritoneal catheter insertion with standard large-volume paracentesis. Both trials are expected to be completed in 2012.	The committee noted that there are 2 ongoing clinical trials using the PeritX peritoneal catheter drainage system. One is investigating the impact on quality of life and the other is comparing early stage PeritX peritoneal catheter insertion with standard large-volume paracentesis. Both trials are expected to be completed in 2012.
Page 13, 4.1	The evidence suggests that the PleurX peritoneal catheter drainage system is a safe and effective alternative to inpatient large-volume paracentesis, is cost saving and reduces hospital bed use.	The evidence suggests that the PeritX peritoneal catheter drainage system is a safe and effective alternative to inpatient large-volume paracentesis, is cost saving and reduces hospital bed use.
Page 13, 4.2	The clinical experts advised the committee that the PleurX peritoneal catheter insertion procedure is unlikely to be more costly to the NHS than the large-volume paracentesis procedure.	The clinical experts advised the committee that the PeritX peritoneal catheter insertion procedure is unlikely to be more costly to the NHS than the large-volume paracentesis procedure.
Page 13, 4.3	The main resource consideration with PleurX is the relative need for community nursing support for the ongoing drainage procedures. However, the committee was advised that the PleurX peritoneal catheter drainage system is unlikely to increase overall community nursing input as was assumed in the cost model (see section 5). This is because most patients in the terminal stages of cancer need community nursing support regardless of the PleurX peritoneal catheter drainage system, and large-	The main resource consideration with PeritX is the relative need for community nursing support for the ongoing drainage procedures. However, the committee was advised that the PeritX peritoneal catheter drainage system is unlikely to increase overall community nursing input as was assumed in the cost model (see section 5). This is because most patients in the terminal stages of cancer need community nursing support regardless of the PeritX peritoneal catheter drainage system, and large-

	volume-paracentesis is associated with a greater need for nursing for overall wound management. Indeed, the committee was advised that it is possible that using the PleurX peritoneal catheter drainage system could lead to an overall reduction in community nursing costs, which would further enhance the resource savings associated with its use.	volume-paracentesis is associated with a greater need for nursing for overall wound management. Indeed, the committee was advised that it is possible that using the PeritX peritoneal catheter drainage system could lead to an overall reduction in community nursing costs, which would further enhance the resource savings associated with its use.
Page 14, 5.1	The sponsor submitted a new cost analysis based on a decision tree model with an embedded Markov model. This model evaluated the costs per patient and system impact of the PleurX peritoneal catheter drainage system for the drainage of treatment-resistant, recurrent malignant ascites in the community setting when compared with inpatient and outpatient large-volume paracentesis.	The sponsor submitted a new cost analysis based on a decision tree model with an embedded Markov model. This model evaluated the costs per patient and system impact of the PeritX peritoneal catheter drainage system for the drainage of treatment-resistant, recurrent malignant ascites in the community setting when compared with inpatient and outpatient large-volume paracentesis.
Page 14, 5.2	The time horizon of the model was 26 weeks (6 months) from the time of the initial PleurX peritoneal catheter insertion. The Markov model was run over 26 weekly cycles to account for the short duration of survival in patients with malignant ascites. The cycles used transition probabilities based on 100% survival at week 0 to 4% survival at week 26. The cost of treatment was multiplied by the transition probability at each cycle; half-cycle corrections were used to incorporate changes in survival within a cycle.	The time horizon of the model was 26 weeks (6 months) from the time of the initial PeritX peritoneal catheter insertion. The Markov model was run over 26 weekly cycles to account for the short duration of survival in patients with malignant ascites. The cycles used transition probabilities based on 100% survival at week 0 to 4% survival at week 26. The cost of treatment was multiplied by the transition probability at each cycle; half-cycle corrections were used to incorporate changes in survival within a cycle.
Page 14, 5.3	The key assumptions used in the model were:	The key assumptions used in the model were:

	• no change in the survival rate in both arms of the model • the need for 2 nurse visits to train patients to self-manage the drainage at home using the PleurX peritoneal catheter drainage system • similar levels of treatment monitoring needs in both arms of the model • a nurse visit length of 15 minutes for the PleurX peritoneal catheter drainage system to help with drainage at home • drainage volume of 9.2 litres per procedure in patients who have repeated large-volume paracentesis • average drainage volume of 3.5 litres per week using the PleurX peritoneal catheter drainage system • one nurse visit per litre of ascitic fluid drained using the PleurX peritoneal catheter drainage system • the cost of re-intervention being equivalent to a first-time catheter insertion procedure.	• no change in the survival rate in both arms of the model • the need for 2 nurse visits to train patients to self-manage the drainage at home using the PeritX peritoneal catheter drainage system • similar levels of treatment monitoring needs in both arms of the model • a nurse visit length of 15 minutes for the PeritX peritoneal catheter drainage system to help with drainage at home • drainage volume of 9.2 litres per procedure in patients who have repeated large-volume paracentesis • average drainage volume of 3.5 litres per week using the PeritX peritoneal catheter drainage system • one nurse visit per litre of ascitic fluid drained using the PeritX peritoneal catheter drainage system • the cost of re-intervention being equivalent to a first-time catheter insertion procedure.
Page 15, 5.4	The model calculated the costs per patient of the	The model calculated the costs per patient of the PeritX

	PleurX peritoneal catheter drainage system and large-volume paracentesis as well as the incremental costs of the PleurX peritoneal catheter drainage system. The costs of the system included: inpatient stay (1 day), procedure consumables and other costs (including staff time), PleurX drainage kits, home nurse visits and treatment of complications (infection, catheter failure and re-intervention). The cost of large-volume paracentesis included: inpatient stay (2.8 days) or outpatient (1 day), procedure consumables and treatment of complications. In addition, the system impact was presented in terms of number of paracentesis sessions, number of litres of ascitic fluid drained, number of bed days, and number of nurse visits for both interventions.	peritoneal catheter drainage system and large-volume paracentesis as well as the incremental costs of the PeritX peritoneal catheter drainage system. The costs of the system included: inpatient stay (1 day), procedure consumables and other costs (including staff time), PeritX drainage kits, home nurse visits and treatment of complications (infection, catheter failure and re-intervention). The cost of large-volume paracentesis included: inpatient stay (2.8 days) or outpatient (1 day), procedure consumables and treatment of complications. In addition, the system impact was presented in terms of number of paracentesis sessions, number of litres of ascitic fluid drained, number of bed days, and number of nurse visits for both interventions.
Page 15, 5.5	The cost per patient for the management of malignant ascites using the PleurX peritoneal catheter drainage system was estimated to be £2,466, whereas for inpatient and outpatient large-volume paracentesis it was estimated to be £3,146 and £1,457 respectively.	The cost per patient for the management of malignant ascites using the PeritX peritoneal catheter drainage system was estimated to be £2,466, whereas for inpatient and outpatient large-volume paracentesis it was estimated to be £3,146 and £1,457 respectively.
Page 15, 5.6	The base-case analysis showed that managing treatment-resistant, recurrent malignant ascites with the PleurX peritoneal catheter drainage system may result in cost saving of £679 per patient when compared with inpatient large-volume paracentesis. In this scenario, 7.4 hospital bed days were saved per patient, but 23.5 more community nurse visits to the patients'	The base-case analysis showed that managing treatment-resistant, recurrent malignant ascites with the PeritX peritoneal catheter drainage system may result in cost saving of £679 per patient when compared with inpatient large-volume paracentesis. In this scenario, 7.4 hospital bed days were saved per patient, but 23.5 more community nurse visits to the patients'

	home were needed. When the PleurX peritoneal catheter drainage system was compared with outpatient large-volume paracentesis, an additional cost of £1,010 per patient was incurred, including 23.5 extra nurse visits but 1.9 fewer hospital bed days used per patient.	home were needed. When the PeritX peritoneal catheter drainage system was compared with outpatient large-volume paracentesis, an additional cost of £1,010 per patient was incurred, including 23.5 extra nurse visits but 1.9 fewer hospital bed days used per patient.
Page 15, 5.7	The key drivers of the new cost analysis were: cost of a hospital bed day, number of bed days per large-volume paracentesis session, number of large-volume paracentesis procedures per month, number of bed days for PleurX peritoneal catheter placement, cost per drainage kit box (10 units), and number of drainage kits used per week per patient. The analysis showed that cost savings associated with the PleurX peritoneal catheter drainage system, when compared with inpatient large-volume paracentesis, were heavily dependent on a reduction in hospital stay. The cost of a bed day was estimated at £312.	The key drivers of the new cost analysis were: cost of a hospital bed day, number of bed days per large-volume paracentesis session, number of large-volume paracentesis procedures per month, number of bed days for PeritX peritoneal catheter placement, cost per drainage kit box (10 units), and number of drainage kits used per week per patient. The analysis showed that cost savings associated with the PeritX peritoneal catheter drainage system, when compared with inpatient large-volume paracentesis, were heavily dependent on a reduction in hospital stay. The cost of a bed day was estimated at £312.
Page 16, 5.8	The sponsor carried out one-way deterministic sensitivity analysis. All variables (except for population size) were tested, and were analysed using a variance of 20% regardless of the level of confidence in an input or the parameter-specific circumstances. Six key drivers were selected and subjected to further deterministic threshold analysis by the external assessment centre across a wide range of values, to identify the point at which the PleurX peritoneal catheter	The sponsor carried out one-way deterministic sensitivity analysis. All variables (except for population size) were tested, and were analysed using a variance of 20% regardless of the level of confidence in an input or the parameter-specific circumstances. Six key drivers were selected and subjected to further deterministic threshold analysis by the external assessment centre across a wide range of values, to identify the point at which the PeritX peritoneal catheter

	drainage system became more costly or cost saving compared with inpatient and outpatient large-volume paracentesis respectively.	drainage system became more costly or cost saving compared with inpatient and outpatient large-volume paracentesis respectively.
Page 14, 5.9	The findings of the threshold sensitivity analysis showed that using the PleurX peritoneal catheter drainage system may incur additional costs when compared with inpatient large-volume paracentesis in the following scenarios: the cost of an excess bed day is reduced to less than £220 per day; the frequency of an inpatient large-volume paracentesis procedure is reduced to fewer than one per month; the average length of inpatient stay after the large-volume paracentesis procedure is decreased to 2.1 days; the number of inpatient bed days following the PleurX peritoneal catheter insertion procedure is increased to more than 3.1 days; the cost of the PleurX drainage kit is increased to more than £915 (per 10 units); more than 5.1 drainage kit units are needed per week. The PleurX peritoneal catheter drainage system may become cost saving when compared with outpatient large-volume paracentesis in the following scenarios: the cost of an excess bed day is increased to more than £825 per day; the frequency of an outpatient large-volume paracentesis procedure is increased to more than 2.5 per month; the average length of hospital stay after the outpatient large-volume paracentesis procedure is increased to more than 2.1 days; the cost of the PleurX drainage kit is decreased to	The findings of the threshold sensitivity analysis showed that using the PeritX peritoneal catheter drainage system may incur additional costs when compared with inpatient large-volume paracentesis in the following scenarios: the cost of an excess bed day is reduced to less than £220 per day; the frequency of an inpatient large-volume paracentesis procedure is reduced to fewer than one per month; the average length of inpatient stay after the large-volume paracentesis procedure is decreased to 2.1 days; the number of inpatient bed days following the PeritX peritoneal catheter insertion procedure is increased to more than 3.1 days; the cost of the PeritX drainage kit is increased to more than £915 (per 10 units); more than 5.1 drainage kit units are needed per week. The PeritX peritoneal catheter drainage system may become cost saving when compared with outpatient large-volume paracentesis in the following scenarios: the cost of an excess bed day is increased to more than £825 per day; the frequency of an outpatient large-volume paracentesis procedure is increased to more than 2.5 per month; the average length of hospital stay after the outpatient large-volume paracentesis procedure is increased to more than 2.1 days; the cost of the PeritX drainage kit is decreased to

	less than £225 (per 10 units); fewer than 1.14 drainage kit units are needed per week.	less than £225 (per 10 units); fewer than 1.14 drainage kit units are needed per week.
Page 16, 5.10	The sensitivity analysis demonstrated that the PleurX peritoneal catheter drainage system is likely to remain cost saving when compared with inpatient large-volume paracentesis and is likely to incur extra costs when compared with outpatient large-volume paracentesis.	The sensitivity analysis demonstrated that the PeritX peritoneal catheter drainage system is likely to remain cost saving when compared with inpatient large-volume paracentesis and is likely to incur extra costs when compared with outpatient large-volume paracentesis.
Page 16-17, 5.11	The new cost analysis showed that the PleurX peritoneal catheter drainage system was cost saving when compared with inpatient large-volume paracentesis, but incurred additional costs when compared with outpatient large-volume paracentesis. The additional costs, compared with outpatient treatment, were incurred mainly from an increased number of home nurse visits, with only a small offset saving in hospital bed days. However, the committee was advised that the additional cost burden imposed on community nursing staff as a result of the PleurX peritoneal catheter drainage system may have been overestimated, given that most patients will receive healthcare in the community regardless of whether or not they have a PleurX peritoneal catheter in place. The committee was advised that many patients may not prefer outpatient to inpatient large-volume paracentesis because it does not necessarily alleviate the intolerable symptoms associated with ascitic fluid	The new cost analysis showed that the PeritX peritoneal catheter drainage system was cost saving when compared with inpatient large-volume paracentesis, but incurred additional costs when compared with outpatient large-volume paracentesis. The additional costs, compared with outpatient treatment, were incurred mainly from an increased number of home nurse visits, with only a small offset saving in hospital bed days. However, the committee was advised that the additional cost burden imposed on community nursing staff as a result of the PeritX peritoneal catheter drainage system may have been overestimated, given that most patients will receive healthcare in the community regardless of whether or not they have a PeritX peritoneal catheter in place. The committee was advised that many patients may not prefer outpatient to inpatient large-volume paracentesis because it does not necessarily alleviate the intolerable symptoms associated with ascitic fluid

	build-up any better than inpatient large-volume paracentesis and yet still creates the need for repeated outpatient visits.	build-up any better than inpatient large-volume paracentesis and yet still creates the need for repeated outpatient visits.
Page 17, 5.12	The committee recognised that large-volume paracentesis is currently offered as an inpatient, outpatient or day case procedure and that practice varies across the UK. Moreover, the resource costs for outpatient and day case large-volume paracentesis differ, with the day case procedure being more costly (although this was not reflected in the cost model). The committee was advised that the PleurX peritoneal catheter drainage system is likely to be cost saving when compared with day case large-volume paracentesis.	The committee recognised that large-volume paracentesis is currently offered as an inpatient, outpatient or day case procedure and that practice varies across the UK. Moreover, the resource costs for outpatient and day case large-volume paracentesis differ, with the day case procedure being more costly (although this was not reflected in the cost model). The committee was advised that the PeritX peritoneal catheter drainage system is likely to be cost saving when compared with day case large-volume paracentesis.
Page 17, 5.14	The committee recognised that the NHS tariff used for the calculation of excess bed days underestimated the cost of an inpatient stay and that correcting this may further increase the cost savings attributable to the PleurX peritoneal catheter drainage system.	The committee recognised that the NHS tariff used for the calculation of excess bed days underestimated the cost of an inpatient stay and that correcting this may further increase the cost savings attributable to the PeritX peritoneal catheter drainage system.
Page 17, 5.15	For the guidance review, the external assessment centre revised the model to reflect 2017 costs (original guidance values are given in brackets). The largest changes were increases in the cost of hospital bed days (£312 to £355) and decreases in the cost of a typical nurse visit (£27 to £14.33). Base-case results for the 2018 revised model shows a cost saving of £1,051 (£679) per patient. The differential cost between	[to be removed]

	PleurX and paracentesis as an outpatient procedure is reduced to an additional cost of £871 (£1,010) per patient. Further details of the 2018 revised model are in the revised model summary [2018].	
Page 17, 5.15 2022 guidance review	-	For the 2022 guidance review, the external assessment centre revised the model to reflect 2020 costs. The largest changes compared to the costs from the 2018 guidance review were increases in the cost of hospital bed days (£355 to £367.78) and decreases in the cost of home visit per hour (£68 to £49). The new costs for the technology were also included. Base-case results for the 2022 revised model (values after first guidance review are given in brackets) show a cost saving of £1,095 (£1,051) per patient. The differential cost between PeritX and paracentesis as an outpatient procedure has increased to an additional cost of £896 (£871) per patient **[2022]**.
Page 18, 6.1	The committee concluded that the PleurX peritoneal catheter drainage system is a clinically safe and effective palliative therapy for the management of treatment-resistant, recurrent malignant ascites, which has the potential to improve quality of life and is cost saving when compared with inpatient large-volume paracentesis.	The committee concluded that the PeritX peritoneal catheter drainage system is a clinically safe and effective palliative therapy for the management of treatment-resistant, recurrent malignant ascites, which has the potential to improve quality of life and is cost saving when compared with inpatient large-volume paracentesis.