NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Medical technology guidance

Assessment report overview

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

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

This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies
- Appendix C: Comments from patient organisations
- Appendix D: Additional submission information
- Appendix E: Sponsor's factual check of the assessment report and the External Assessment Centre's responses

1 The technology

The PleurX peritoneal catheter drainage system (UK Medical Ltd) allows the repeated drainage of ascitic fluid in the community setting. It is intended for

use in the palliative management of treatment-resistant, recurrent malignant ascites.

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 within 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 it. This reduces the risk of subsequent infection and leakage of peritoneal fluid.

The proximal end of the PleurX 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. 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 dressing over the catheter.

The PleurX peritoneal catheter can remain in place indefinitely and patients and carers are trained to perform fluid drainage themselves as and when needed. For draining fluid, the vacuum bottle is attached to the catheter and a fresh valve cap and dressing are re-applied once the drainage is completed. For the majority of the time, the catheter is coiled up and covered with a gauze pad and waterproof dressing.

2 Proposed use of the technology

2.1 Disease or condition

Malignant ascites is defined as abnormal accumulation of fluid in the peritoneal cavity caused by cancer. It occurs in association with a variety of cancers especially breast, bronchus, ovary, stomach, pancreas and colon cancer (Becker et al. 2006). The accumulation of a large-volume of ascitic

fluid increases abdominal pressure and can cause symptoms such as bloating, nausea, acid reflux, reduced appetite, negative perception of body image, and psychological distress (Becker et al. 2006). Patients with malignant ascites have a mean survival of 1–4 months, depending on the nature and extent of the underlying tumour (Courtney et al. 2008). This may be significantly longer in patients having palliative treatment.

2.2 Patient group

The PleurX peritoneal catheter drainage system is intended for use in patients with recurrent malignant ascites that is resistant to medical management. There are no data available on the prevalence of treatment-resistant, recurrent malignant ascites in the UK. However, Hospital Episode Statistics (HES) main procedures and interventions data for 2009–10 report that 16,821 patients underwent abdominal paracentesis to drain ascitic fluid from the peritoneal cavity for both diagnostic and therapeutic indications. Malignant ascites accounts for approximately 10% of all ascites cases.

2.3 Current management

The conventional management of patients with treatment-resistant, recurrent malignant ascites involves multiple large-volume paracentesis procedures that are carried out in hospital. Paracentesis involves inserting a catheter into the peritoneal cavity to drain ascitic fluid. During large-volume paracentesis more than 5 litres of ascitic fluid is removed in one go.

2.4 Proposed management with new technology

The PleurX peritoneal catheter drainage system can be offered for draining ascitic fluid in patients with treatment-resistant, recurrent malignant ascites who are considered suitable for large-volume paracentesis. The initial catheter placement procedure can be performed under local anaesthesia in an outpatient setting using ultrasound guidance, and follows the same principles as placing a catheter for abdominal paracentesis. Subsequent drainage procedures can be performed intermittently in the community setting using

1 litre PleurX vacuum bottles with drainage kit as and when needed, by patients, their carers or community nurses.

2.5 Equality issues

No equality issues were identified.

3 Issues for consideration by the Committee

3.1 Claimed benefits

The benefits to patients claimed by the sponsor are:

- repeated drainage of ascitic fluid in community settings may allow for greater patient independence and the flexibility to fit the drainage procedure into their daily lives
- frequent drainage of smaller quantities of ascitic fluid may result in better control of symptoms associated with the accumulation of large amounts of ascites, that is, breathlessness, nausea, bloating, acid reflux, abdominal pain, early satiety, reduced mobility and psychological distress related to body image
- reduced need for repeated large-volume paracentesis procedures and the associated infection risk.

The benefits to the healthcare system claimed by the sponsor are:

- resource savings through a reduced need for hospital nurse and physician time, outpatient visits, and hospital bed days.

3.2 Main issues

The available clinical evidence suggests the PleurX peritoneal catheter drainage system has good technical success, comparable complication rates to large-volume paracentesis, and remains in place for over 10 weeks on average. Patients reported that the PleurX peritoneal catheter drainage system was a convenient alternative to large-volume paracentesis and

showed improvements in symptom control. In general, the evidence is based on observational studies, with very limited comparative data.

The limited comparative evidence suggests that the PleurX peritoneal catheter drainage system is a safe and effective alternative to inpatient large-volume paracentesis, is cost saving and releases hospital bed days.

There is some uncertainty about the number of patients who could be treated using PleurX, and the proportion of patients currently treated using-large-volume paracentesis in inpatient and outpatient settings. The sponsor contacted NHS clinicians to ask them to complete a key opinion leader questionnaire. Two completed questionnaires were received, in which inpatient large-volume paracentesis-treated cases were estimated at 50% and 64.2% of all patients with treatment-resistant, recurrent, malignant ascites who need the frequent drainage of ascitic fluid. However, these values were not built into the sponsor's model. Any variation in the proportion of inpatient and outpatient large-volume paracentesis procedures carried out in the NHS may affect the population-level cost savings from using the PleurX peritoneal catheter drainage system, because it incurs extra costs when compared with outpatient large-volume paracentesis.

Differences in study design indicate that there is uncertainty about the care pathway point at which it would be clinically appropriate to treat patients with treatment-resistant, recurrent malignant ascites with PleurX. For example, Tapping et al. (2011) considered that patients for whom the PleurX peritoneal catheter drainage system is suitable are those who have had at least three previous conventional paracentesis procedures. Courtney et al. (2008) included only those patients who have had at least two conventional paracentesis procedures in the previous 30 days.

Economic evidence showed that the PleurX peritoneal catheter drainage system was cost saving when compared to inpatient large-volume paracentesis, but incurred an additional cost 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 additional burden imposed on community nursing staff because of the PleurX peritoneal catheter drainage system may have been overestimated, given that some patients may receive community healthcare regardless of whether they have a PleurX peritoneal catheter drainage system.

In the scenario comparing the PleurX peritoneal catheter drainage system with inpatient large-volume paracentesis, the External Assessment Centre considered several model inputs to be conservative estimates. In particular, the frequency of inpatient large-volume paracentesis per month, which was the key cost driver. By changing the value from 1.22 inpatient large-volume paracentesis procedures per month used in the base-case analysis to 2.8 as reported by Courtney et al. (2008), the cost saving associated with the PleurX peritoneal catheter drainage system increased to £3381 per patient when compared with inpatient large-volume paracentesis. The number of community nurse visits per week for assisted PleurX peritoneal catheter drainage system patients was considered to be an overestimation.

The sponsor used rates of infection (7.5%) and catheter failure (7.5%) from a single study (Rosenberg et al. [2004]). However, there was a wide range of complication rates across PleurX-only studies, which ranged from 0% (Saiz-Mendiguren et al. [2010]) to 59% (Courtney et al. [2008]). A 4% re-intervention rate (removal and replacement of the PleurX peritoneal catheter) (Mullan et al. [2011a]) was used in the model, but Tapping et al. (2011) reported a 12.5% re-intervention rate from inadvertent displacement of the catheter. Sensitivity analysis of the variation in the PleurX peritoneal catheter drainage system complication and re-intervention rates found them to be of low impact, and the PleurX peritoneal catheter drainage system remained cost saving when compared with inpatient large-volume paracentesis.

A small number of studies support the claim of improved quality of life for patients with malignant ascites. This is chiefly owing to avoidance of hospital

inpatient stays for conventional paracenteses, and improved control of the symptoms of ascites by regularly removing small volumes of fluid, and thus avoiding the problems associated with massive fluid accumulation.

4 The evidence

4.1 Summary of evidence of clinical benefit

The clinical evidence for the PleurX peritoneal catheter drainage system is based on nine observational studies (ten manuscripts), two of which were based in the UK. Six studies were case series with ten or more patients, one study was a qualitative case series (four patients), and there were three case reports (four or fewer patients).

Rosenberg et al. (2004) evaluated treatment complication rates in patients with malignant ascites managed with the PleurX peritoneal catheter drainage system (n = 40 patients and catheters) and conventional large-volume paracentesis (n = 67 patients, 392 procedures) in a single-centre, retrospective, comparative case series. Overall complication rates (using patient numbers rather than number of procedures) were the same for both procedures: 7.5% (3 of 40; 95% CI 1.6% to 20%) for the PleurX peritoneal catheter drainage system and 7.5% (5 of 67; 95% CI 2.2% to 15%) for large-volume paracentesis. In patients whose ascites were managed with PleurX, complications were caused by infection (n = 1), leakage (n = 1), and loculations (n = 1) and all catheters were subsequently removed. Large-volume paracentesis complications were caused by peritonitis (n = 3) and loculations (n = 2). The PleurX peritoneal catheter patency (defined as the number of catheters functioning at death, study end, or resolution of ascites) was 67.5% (n = 27); however 11 (27.5%) patients were lost to follow-up.

Courtney et al. (2008) evaluated treatment outcomes in 34 patients with malignant ascites treated with the PleurX peritoneal catheter drainage system over a 12 week follow-up period (and until death in some patients) in a multi-centre, single arm, prospective case series. They reported 100% technical

success (defined by intraperitoneal positioning of the device and the ability to withdraw ascitic fluid from the device at the completion of the procedure) during the placement procedure except for one minor procedural complication. The overall complication rate over the course of use was 59% (n = 20) including minor complications that resolved spontaneously. Two catheters needed to be removed, and other complications included infection (n =2), occlusion/loculations (n = 4), leakage of ascitic fluid (n = 7), dizziness (n = 5), shortness of breath (n = 1) and severe anaemia (n = 1). Available records from 19 patients showed that the mean number of drainage sessions after placement of the PleurX peritoneal catheter was 23.3 per patient (range 5–56), and that of the total 433 sessions, 13% were performed by a nurse, the remainder were carried out by the patient alone (28%) or a carer (58%). Catheter patency rate was 85% (n = 29); the remaining five patients were lost to follow-up. Changes in symptom severity at 2, 8 and 12 weeks compared with baseline measurement were assessed using a validated tool. There was a reduction in the severity of abdominal discomfort, bloating, diarrhoea and nausea at 2 and 8 weeks but an overall improvement in quality of life at 12 weeks was reported in only 28% of respondents. The lack of control data limits the interpretation of this evidence.

In a single-arm retrospective case series study, Mullan et al. (2011a) evaluated the procedural safety, long-term efficacy, long-term complication profile and cost benefit of the PleurX peritoneal catheter drainage system in the management of recurrent malignant ascites (n = 50 patients, 52 catheters). Two patients had their catheters re-inserted. The study reported 100% procedural success with no procedural morbidity or mortality. It reported a mean survival of 59.4 days (range 4–216 days) and 165 days (range 29–1036 days) after PleurX peritoneal catheter insertion and after first conventional paracentesis respectively. On average, 5.3 conventional drainage procedures were performed before PleurX peritoneal catheter insertion. Average ascitic fluid drainage per episode of paracentesis per person was 9.2 litres. Average hospital stay for patients having a conventional

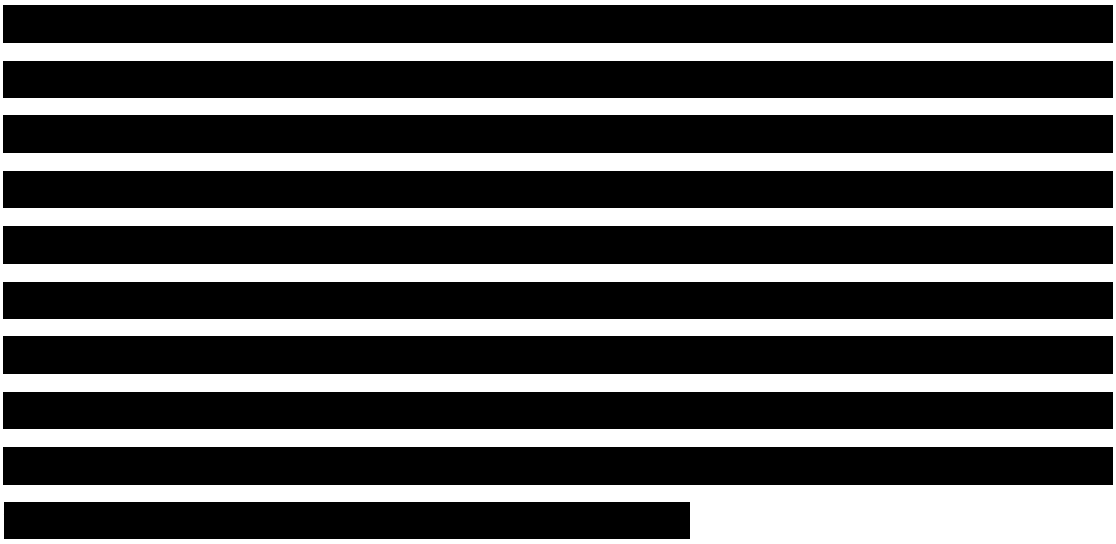
paracentesis procedure was 2.8 days (range 1–6 days; n = 23). Eight patients (16%) experienced complications including peritonitis (n = 1), lymphangitis (n = 1), occlusion/loculations (n = 3), ascitic leakage (n = 1), displacement (n = 1) and pain (n = 1); one catheter needed to be removed. Primary or secondary catheter patency at death was 100% with management of complications augmented by multi-modality imaging and fibrinolysis of malfunctioning catheters.

Richard et al. (2001) evaluated the outcomes of the PleurX peritoneal catheter drainage system in patients with treatment-resistant, recurrent malignant ascites in a single-arm retrospective case series study (n = 10 patients and catheters). They reported 100% procedural success. Two patients experienced complications (20%), which were occlusion/loculations (n = 1) and displacement (n = 1). The average time catheters remained in place was 70 days (range 1–100 days).

Tapping et al. (2011) evaluated the outcomes of the PleurX peritoneal catheter drainage system in patients with treatment-resistant, recurrent malignant ascites in a single-arm retrospective case series (n = 28 patients, 32 catheters). Technical success was 100% and 12 complications (28%) were reported. Complications were minor catheter site infections (n = 5), ascitic leakage (n = 1), displacement (n = 4), hernia (n = 1), and one complication had no further information. No catheters needed to be removed other than those inadvertently dislodged. The average time catheters remained in place was 113 days (range 5–365 days) and catheter patency was 86% (24/28).

Saiz-Mendiguren et al. (2010) conducted an observational descriptive case series study (n = 10 patients) managed with the PleurX peritoneal catheter drainage system. The study analysed the duration of the procedure, pain reported by the patient during the procedure (using the visual analogue scale [VAS] score), short- and long-term complications, median patency of the catheter, and the volume of ascitic fluid drained at home (reported by telephone or during consultation). The technical success rate was 100% with

the PleurX peritoneal catheter insertion procedure but two patients reported discomfort during the procedure (VAS scores 2 and 3). No complications were reported during or after the procedure. In one patient with generalised sepsis thought to be caused by a venous cannula, the PleurX peritoneal catheter was removed 58 days after placement as a precaution. Catheters remained patent for a median of 52 days (range 13–113 days) in the 9 patients who died. The mean time catheters remained in place was 52 days (range 13–113 days). One patient remained alive with a patent catheter 124 days after placement at the end of the study. The patient (or their relatives) reported mean drainage volume of the ascitic fluid was around 1 litre (1 vacuum bottle) every 2–10 days.



Three case reports relevant to the decision problem were also identified. Brooks et al. (2006) described one patient who had a PleurX peritoneal catheter in place for 18 months and developed three complications. Iyengar et al. (2002) described three patients who had catheters in place for 6, 7, and 12 weeks. One patient experienced dehydration, and one catheter was removed as a precaution from a patient with sepsis. Mullan et al. (2011b) was a case report of four patients from the main study (Mullan et al. 2011a), and described their treatment for loculations with streptokinase fibrinolytic therapy.

4.2 Summary of economic evidence

Mullan et al. (2011a) presented a cost–benefit analysis of treating a patient with malignant ascites with conventional paracentesis versus the costs of using the PleurX peritoneal catheter drainage system from an NHS secondary care perspective. Costs included equipment and consumables, procedure costs and inpatient stay. The authors showed that replacing repeated paracentesis with the PleurX peritoneal catheter drainage system to manage malignant ascites may result in potential cost savings of £2573 per patient. However, the costs of providing nursing care at home in the PleurX peritoneal catheter drainage system arm and the costs of complications were not included in the analysis.

New cost analysis

The sponsor submitted a new cost analysis based on a decision tree model with an embedded Markov model. This evaluated the costs per patient and system impact of the PleurX peritoneal catheter drainage system for the drainage of treatment resistant, recurrent malignant ascites at home when compared with inpatient and outpatient large-volume paracentesis.

The time horizon of the model was 26 weeks (6 months) from the time of initial PleurX peritoneal catheter insertion. The Markov model was run over 26 weekly cycles to account for the short duration of survival of 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 did not take into account the treatment period before PleurX peritoneal catheter placement, which is likely to include several conventional paracenteses.

The key assumptions used in the model were:

- no change in the survival rate in both arms of the model

- the need for two 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 to help with drainage at home
- drainage volume of 9.2 litres per episode 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 is equivalent to a first-time catheter insertion procedure.

The External Assessment Centre considered that there were some limitations of the model. It considered that complications associated with patients who only have large-volume paracentesis were not adequately considered. Treatment of complications was assumed to be the same between the PleurX peritoneal catheter drainage system and large-volume paracentesis. The sponsor used ‘catheter failure’ as an aggregate term for complications other than infection, which were treated using streptokinase for occlusion or loculation. The model did not consider costs for complications that did not resolve after a single treatment. In addition, the model did not include patients whose malignant ascites resolved after placement of the PleurX peritoneal catheter.

Costs and benefits

The model calculated the costs per patient of the PleurX peritoneal catheter drainage system and large-volume paracentesis as well as the incremental costs of the PleurX. The costs of the PleurX peritoneal catheter drainage 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.

The list price for the PleurX peritoneal catheter is £245 per unit and for the PleurX drainage kit with 1 litre vacuum bottle the list price is £64 per unit.

The cost per patient for the management of malignant ascites using the PleurX peritoneal catheter drainage system was estimated to be £2466, whereas for inpatient and outpatient large-volume paracentesis it was estimated to be £3144 and £1457 respectively.

The key drivers of the new cost analysis were: cost of a hospital bed day, number of bed days per large-volume paracentesis session, frequency of large-volume paracentesis 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 of the PleurX peritoneal catheter drainage system, when compared with inpatient large-volume paracentesis, were heavily dependent on the reduction in the hospital stay. The cost of a bed day was estimated as being £312 (NHS reference costs 2009–10 for an excess bed day).

The costs used as inputs in the model were derived mostly from the Mullan et al. study (2011a). Two key clinical variables, mean patient survival and complication frequency were extracted from Mullan et al. (2011a) and Rosenberg et al. (2004) respectively. Healthcare resource data were derived from a range of studies. Data from one of the two completed key opinion leader questionnaire obtained by the sponsor was used as an input for the number of nurse visits required to train each patient to use the PleurX peritoneal catheter drainage system.

Results

The base-case analysis showed that managing 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 meant an extra 23.5 community nurse visits to patients' homes were needed.

When the PleurX peritoneal catheter drainage system was compared with outpatient large-volume paracentesis in the base-case analysis, there was an additional cost of £1010 per patient, as well as 23.5 extra nurse visits. In this scenario, the PleurX peritoneal catheter drainage system would save 1.9 hospital bed days per patient.

One-way deterministic sensitivity analysis was carried out. 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 wider range of values, to identify the point at which the PleurX peritoneal catheter drainage system became more costly or cost saving compared with inpatient and outpatient large-volume paracentesis respectively.

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 hospital stay is reduced to less than £220 per day
- the frequency of an inpatient paracentesis procedure is reduced to fewer than one per month
- length of average inpatient stay after the large-volume paracentesis procedure is decreased to 2.1 days
- number of inpatient bed days following the PleurX peritoneal catheter insertion procedure is increased to more than 3.1 days
- the cost of the 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 hospital stay is increased to more than £825 per day
- the frequency of an outpatient paracentesis procedure is increased to more than 2.5 per month
- length of average inpatient stay after the outpatient large-volume paracentesis procedure is increased more than to 2.1 days
- the cost of drainage kit is decreased to less than £225 (per 10 units)
- fewer than 1.14drainage kit units are needed per week.

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.

5 Ongoing research

‘An Early Safety and Efficacy Study of Ascites Management: Standard Paracentesis or Early Intervention with PleurX Catheters in Patients with Malignant Ascites’ (clinical trial ID NCT01077063). This trial is currently recruiting participants and is expected to be completed in 2012 (as of July 2011). It is a controlled prospective trial of the safety and efficacy of ascites management, and will be looking at standard paracentesis and early intervention with the PleurX peritoneal catheter drainage system in patients with malignant ascites. The trial aims to recruit 15 patients in each arm.

‘Impact of Palliative Catheter Placement on the Quality of Life of Patients with Refractory Ascites’ (clinical trial ID NCT01188746). This trial has completed recruitment (n = 50 patients) and is expected to be completed in 2012. This trial aims to explore the impact of palliative catheter placement on the quality of life of patients with refractory ascites. Quality of life will be measured by the McGill Quality of Life Questionnaire and the European Organization for Research and Treatment of Cancer Quality of Life Core Questionnaire.

6 Authors

Mukesh Dhariwal, Analyst

NICE Medical Technologies Evaluation Programme

October 2011