National Institute for Health and Care Excellence

IP998/2 Subcutaneous automated low-flow pump implantation for refractory ascites caused by cirrhosis

IPAC 09/08/18

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 British Liver Trust	**General**	Comments from the British Liver Trust on behalf of patients: Ascites is a build-up of fluid between the two layers of the peritoneum. The most common cause of ascites is advanced liver disease or cirrhosis. The fluid can accumulate slowly over weeks or months and can be painful, especially if the fluid becomes infected and requires urgent medical attention. Symptoms can range from difficulty breathing when lying down, to nausea and vomiting, abdominal pain and diminished appetite. Refractory ascites is defined as ascites that does not recede or that recurs shortly after therapeutic paracentesis, despite sodium restriction and diuretic treatment (Senousey and Draganov 2009) Patients with refractory ascites have a poor prognosis and current treatment options are limited to include large volume paracentesis, albumin infusion and insertion of a transjugular intrahepatic portosystemic shunt. Ascites is the most common major complication of cirrhosis and is an important landmark in the natural history of chronic liver disease. If observed for 10 years, approximately 60% of patients with cirrhosis develop ascites requiring therapy. The survival rate 5 years after ascites	Thank you for your comment. Section 3.7 of the guidance states: 'The committee was informed that after the procedure patients need regular monitoring, and they may need infusions of albumin.' The committee has added a committee comment, stating that the procedure has the potential to improve the quality of life for patients with refractory ascites, and their families or carers.

			develops is only 30-40%. (Chalasani and Vuppalanchi 2013) The British Liver Trust's nurse led helpline has received many calls from people suffering with ascites, it has a huge effect on quality of life and people report feelings of isolation and depression as they cannot mobilise or often meet their own activities of daily living. Family members also contact our helpline to discuss their sense of helplessness having to take their loved ones into hospital for constant drains and trying to manage them at home. The British Liver Trusts online community currently has 12,400 forum members. Refractory ascites is a topic that is often discussed. Some recent examples; **-'I'm being drained weekly now- how can I continue like this?'** **-'My belly was huge, it made me exhausted and breathless and I couldn't eat properly, I kept begging them to take the fluid out'** **-'I was drained 6 litres a week for 8 months but after every drain it was back within two days'** The British Liver Trust recognises the impact of treating ascites not only on the patient and family, but also the increasing re-admission rate into hospital for paracentesis. We therefore welcome NICE'S Interventional Procedures Consultation which has now issued draft guidance on the use of the Subcutaneous automated low flow pump implantation for refractory ascites. The Trust has reviewed the existing research and is enthused by the possible reduced hospital admissions and improved quality of life for the patients who may be offered this device as a part of a clinical trial.	

			The British Liver Trust understands the documented clinical risks to using this device and would call for very close monitoring by senior specialist hepatologists. Liver disease is the third largest cause of premature death and numbers are rising each year. For patients with refractory ascites there are often no alternatives to treatment other than constant invasive paracentesis. The British Liver Trust therefore supports further research into the use of this device in the hope it can alleviate some of the suffering caused by ascites.	
2	Consultee 2 NHS Professional	**General**	TIPSS and/or Liver Transplant should remain the primary treatment options for patients with refractory ascites. Alfapump insertion should only be considered in patients who are not suitable for TIPSS or transplant and those with reasonable renal function (so as to allow patients to remain at home, rather than repeated attendances for albumin infusions which does not improve on repeated attendances for LVP). Patient selection for alfapump should only be performed in centres who can assess patients' suitability for definitive and more successful therapies such as transplant or TIPSS insertion.	Thank you for your comment. Section 3.8 of the guidance notes that most of the published evidence on the procedure only included patients for whom a transjugular intrahepatic portosystemic shunt is unsuitable. Section 1.4 of the guidance has been changed to include mention of specialist centres. Section 1.5 of the guidance states that further research should report details of patient selection.
3	Consultee 2 NHS Professional	**General**	Alfapump should not be compared to Transplant or TIPSS as it is not a definitive procedure, but rather a method of palliation to improve quality of life, and clear patient selection criteria should be developed.	Thank you for your comment. The randomised controlled trial discussed by the committee compared the procedure with large volume paracentesis. The committee has added a committee comment, stating that the

				procedure has the potential to improve the quality of life for patients with refractory ascites, and their families or carers.
4	Consultee 3 British Association for the Study of the Liver	**General**	Subcutaneous automated low-flow pump implantation for refractory ascites caused by cirrhosis In development [GID-IPG10082] Many thanks for giving BASL an opportunity to comment on the recent consultation document evaluating the subcutaneous automated low-flow pump for refractory ascites in cirrhosis. BASL feel that NICEâ€™s decision to advise that this procedure should be considered still research seems appropriate and considered following a review of the 1 randomised control trial and 6 cases series studies available in the medical literature. We also agree with what research data should be captured as part of these research studies. We feel the important points raised in this document below are vital for patient and device safety and are fully endorsed by BASL. These include: 1. NHS Trusts should have oversight of this technology through clinical governance committees 2. Pre procedure checklists should be followed to minimise the potential risks of device insertion	Thank you for your comment. Section 1.1 of the guidance states that the procedure should only be used with special arrangements for clinical governance, consent, and audit or research. This main recommendation has changed from the original guidance, which stated that the procedure should only be used in the context of research. Cost-effectiveness is not part of the remit of the IP Programme.

			3. All device failures should be reported to the MHRA 4. All procedures should be audited. Audit data should include mode of insertion (Surgical or IR), duration of patient stay, TOTAL costs including admissions for â€œPump paracentesisâ€, use of albumin, antibiotics etc. Data on patient selection is also critical considering the 50% 1 year mortality of diuretic resistant ascites in the TIPS paper by Bureaux. (Gastroenterology. 2017 Jan;152(1):157-163.) [redacted]	
5	Consultee 4 Liver4Life	**General**	We see this technology as a real benefit to patients who are affected by Ascites. In many cases it is a real life changer, and we would like to this this as a standard of care for suitable patients. Any intervention that makes treatment of ascites simpler and less invasive is welcome. Our only concern is the number of pump failures and we hope that this would be addressed by the manufacturer as a key issue.	Thank you for your comment. The committee has added a committee comment, stating that the procedure has the potential to improve the quality of life for patients with refractory ascites, and their families or carers.
6	Consultee 5 NHS Professional LTHT	**General**	I have referred a number of patients for consideration of this procedure as the Unit I work in does not currently offer this service, but has previously carried out a pump insertion. I think patient selection is crucial and it is vital that patients are counselled correctly. I therefore agree that this should only be done in level 2/3 Hepatology centres, where Consultants have experience of managing patients with liver failure and assessing patientsâ€™ suitability for TIPSS/liver transplant. This is not a life-saving procedure and in my experience, it's	Thank you for your comment. Section 1.4 of the guidance has been changed to include mention of specialist centres. The published evidence describes a number of patients who have had a liver transplant after the procedure.

			use lies in the palliative setting only, when patients are deemed unsuitable for TIPSS or liver transplant. With the current level of evidence, I don't think it should be used as a bridge to transplantation, given the potential adverse events, that may then render a patient ineligible for transplantation. In my practice, there are a number of patients that would wish to pursue the option of a pump, rather than continue with large volume paracentesis. For suitable patients, it could dramatically improve their quality of life and allow for improvements in nutrition. Given the costs incurred with regular admission (even to a day case unit) for paracentesis, I think the costs are offset if the pump works, the patient survive >6/12 and there are no on-going complications.	Cost-effectiveness is not part of the remit of the IP Programme.
7	Consultee 6 Specialist adviser	**1.1**	Thank you for alerting me to this preliminary guidance I think you have managed to marry the tension between adopting a new technology with its problems whilst also recognising the need for innovation in this area. It should be borne in mind that the quality of life for patients with the pumps appears to be higher despite the problems as patients are able to maintain a degree of independence. The alternatives (paracentesis or tunnelled drains) are not ideal and lead to a rapid loss of patient condition	Thank you for your comment. The consultee agrees with the main recommendation. The committee has added a committee comment, stating that the procedure has the potential to improve the quality of life for patients with refractory ascites, and their families or carers.
8	Consultee 6 Specialist adviser	**1.4**	I agree that only liver failure centres should be allowed to offer this service as the unit should have access to all the alternatives, including TIPSS, but this would not need to include transplantation. It is vital that the patient remains the	Thank you for your comment. Section 1.4 of the guidance has been changed to include mention of specialist centres.

			responsibility of the unit where the pump is implanted and does not get lost to follow up.	
9	Consultee 6 Specialist adviser	**General**	Whilst I agree with the concerns, there does need to be some recognition that for many patients developing decompensated cirrhosis >70 years there is no existing technology or drug that will improve their quality of life. Whilst there is still a lot to learn about AlfaPumps, the lack of any real therapeutic alternative mandates that we explore these technological developments to understand in whom they work best. As long as patients are made aware that they will be contributing to that learning process and that the information is collected in a robust manner I think it is very reasonable to support the use of this technology in the NHS within appropriate units.	Thank you for your comment.
10	Consultee 7 Company Sequana Medical	**3.5**	The majority of the published evidence, as referred to in 3.5 is based on older data, the majority of these patients were enrolled (and thus treated) up to 10 years ago. We do agree that in some of these published studies, the incidence of failure is higher than what we would consider desirable, also after consultation with the expert we interact closely with (heptalogists and surgeons-implanters). However, we have seen a favorable evolution of such events, which is considered typical for “medical device evolution”, which is leading to currently a significantly lower number of reinterventions for system issues (the graph that was provided with the submission, non-published data, data on file from Sequana Medical). This trend of reduction over time, shows that the current stable rate of such reinterventions comes from approximately 40% (which was at the time of the above mentioned studies) to 12-15 % at this time. This rate has been estimated by the expert we	Thank you for your comment. A committee comment has been added, stating: ‘The committee was informed that the technology for this procedure is evolving.’ A new paper has been added to table 2 of the overview, which reports the use of a modified catheter in a small number of patients.

			consult with as a rate which they consider “acceptable” since this is a patient population with significant comorbidities. It is important to note that this reduction is the results of some changes to the system (eg the old version of the peritoneal catheter was changed for a new design, which resulted in no reports of peritoneal catheter clogging anymore), another reason why we see the important reduction in such events and the improvement in clinical outcomes is because, with the support of experts, we can provide better recommendation for the implementation of this therapy (eg patient follow up etc). This is currently being formalized by the development (and implementation) of “careprotocols”: expert en experienced alfapump users have held several meetings and agreed on expert recommendations. Once these are published, this will provide further guidance to physicians when considering the alfapump (pre-implant care, the implant procedure and post implant and long term follow up).	
11	Consultee 7 Company Sequana Medical	**3.6**	The increase in acute kidney failure: this can be multifactorial: the patient population is most certainly at risk for such events. Also, in the studies, the use of albumin for patients receiving the alfapump was not recommended, while this was the case for patients receiving standard of care. With the current evidence on the protective effect of albumin in patients with advanced cirrhotic disease (the recently published “ANSWER” study), we believe patients with the alfapump might also benefit and this might be protective against the development of renal complications. It is however important to note that such renal events were generally low grade and responded to routine management with resolution of signs and symptoms after a short period.	Thank you for your comment. Section 3.7 of the guidance notes that patients may need infusions of albumin. The committee discussed this comment but decided not to change the guidance.
12	Consultee 7 Company	**3.7 and 3.8**	Sequana Medical currently has several projects in its clinical development plan, one project would seek to find an answer	Thank you for your comment.

	Sequana Medical		on the benefit of Albumin in patients that are on alfapump treatment, and we are currently in the start-up phase of a very large post market registry, that will be of an observational nature and will collect data on “real world” use of the alfampump. We expect that there might be a significant number of patients that could have been candidate for a TIPS procedure but in whom the treating physician would have considered the alfapump. Collection of such registry data is believed to be very valuable and for that reason Sequana Medical is very supportive for this kind of (additional and supplementary) evidence generation.	Section 3.7 of the guidance notes that patients may need infusions of albumin. Section 1.5 of the guidance states that ‘Further research should report details of patient selection, the frequency of pump-related complications, and whether regular albumin infusions are needed.’ The guidance for this procedure may be reassessed when relevant new research is published.
13	Consultee 8 NHS Professional	**General**	I see you are reviewing this device. I have implanted about 6 of these. I would suggest that the publications that were cited before partly missed the point when the discussions of costs arose. I don’t think its correct to compare modes of treatment when it comes to the alfa pump because it should be viewed as a useful technique when all that there is available are recurrent paracentesis. When we had to obtain funding from Primary Care groups to pay for the pump what really made the argument was the time line and admissions for paracentesis. All of the patients had gone down the medical management routes and whether or not to transplant the liver. The few patients who at the end of it all may be had renal impairment which meant that diuretics had to be restricted or right cardiac failure and were having a miserable life with admission every two weeks for paracentesis and documented regular admissions 10+ for paracentesis quite clearly had no alternative and these were good candidates for the alfa pump and it made their terminal care easier.	Thank you for your comment. The IPG supports the use of this procedure with special arrangements in carefully selected groups of patients. The IP programme does not consider costs.

understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."