Northern Treatment Advisory Group

Northern (NHS) Treatment Advisory Group

Treatment Appraisal: Decision Summary

Date	**22nd November 2016 (updated 4th June 2019) (reviewed 22nd February 2022 & no changes made)**
Appraisal & Details	**Alfapump® device** The Northern (NHS) Treatment Advisory Group considered an appraisal of the **Alfapump® device for ascites due to liver cirrhosis.**
Recommendation	**The Northern (NHS) Treatment Advisory Group recommends the use of Alfapump® for refractory ascites caused by advanced liver disease as recommended by specialists for patients that fulfil the following criteria:** *Those with refractory ascites (due to portal hypertension) with preserved liver synthetic function who has a contra indication to the TIPSS (transjugular intrahepatic portosystemic shunts) procedure and are not suitable for a liver transplant. Patients should have a likely expected survival of >6 months and are likely to be having very regular (every 2 weeks) paracentesis.* The group recommends that, in line with NICE IPG 631 recommendations, specialists should audit the use of the Alfapump® and they should clearly document the indications for use of the procedure and details of patient selection. Reported outcomes should include quality of life, overall survival and paracentesis-free survival, duration of function of the drainage system, nutritional parameters and any complications associated with its implantation or use. The Alfapump® system received a CE in July 2011 for its use in liver disease.
Clinical evidence summary	Three published studies support the use of the Alfapump® system, including one small, open-label randomized trial in 60 patients at seven centres in five European countries. Patients were adults with liver cirrhosis and refractory ascites requiring periodic large volume paracentesis (LVP), who were not eligible for TIPSS. Alfapump® was compared to standard care, and the primary outcome was time to first LVP. Median time to first LVP was 15 days in the standard care arm, and was not reach in the Alfapump® group (hazard ratio 0.13, p<0.001). The standard care group also required significantly more LVP procedures (mean 1.1 vs. 8.2, p<0.001). Additionally, a non-randomized study was conducted in 56 patients at ten centres in four European countries. Patients were adults with refractory ascites for whom TIPSS was contraindicated. Follow-up was planned for 24 months, however only 3 patients had completed this follow-up at the time of publication. Twenty-three patients died during the study, and seven died after withdrawing due to pump removal. Mean survival was 12.8 months, and the primary cause of death was progression of cirrhosis. Frequency of LVP was reduced from a mean of 2.9 per month to 0.3, and mean LVP volume decreased from 19.3 to 1.2 litres per month. In total 37 patients (66%) did not require further LVP after receiving the pump.

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	Finally, the Pioneer study was a non-randomized trial to assess the safety and efficacy of the Alfapump® in the management of refractory ascites. The study enrolled 40 patients at nine centres in four European countries and patients were followed-up for 6 months after the insertion of the pump. The Alfapump® was successfully inserted into all forty patients. In total, the 40 implanted Alfapump® systems removed 4630 L of ascitic fluid over 4659 patient days, a mean of 0.99 L per patient per day. The median number of paracentesis performed in the month preceding Alfapump® implant was 3.4 (range 1–6) which dropped to 0.24 (range 0–5) per month after implant (p <0.01); 40% of the patients had no paracentesis after receiving their pump. Overall, there was a 90% reduction in the volume of ascitic fluid removed by paracentesis. The majority of other trial data are only available in conference extracts and have not yet been fully published. Studies are ongoing to look at improvements in quality of life in patients with the Alfapump® device.
Safety	There are limited safety data available on the use of the Alfapump® device. In general, safety issues associated with the Alfapump® include catheter occlusions, infections of the pump pocket, and pump malfunctions. The randomized study reported that seven patients required intervention for a problem with the Alfapump® device, of whom six required component replacement or repositioning and three required removal of the device. Acute kidney injury was more common with Alfapump® than standard care (29 vs. 11, p=0.007). Falls in serum albumin were more common with Alfapump® The most frequent adverse events in the first non-randomized study were clogging of the peritoneal catheter (21 events in 13 patients). Seventeen patients required at least one additional intervention, of whom eleven had a pump replacement. The pump was removed in 27 patients, including 9 who received liver transplants and 17 who had serious adverse events due to liver disease. The PIONEER study reported that 9 patients (22.5%) had 10 SAEs related to the bladder catheter. There were 5 bladder catheter dislodgements in 5 patients (12.5%), 4 cases of prolapse of the bladder catheter into the urethra in 3 patients (7.5%), and one bladder catheter that became kinked, and requiring repair (2.5%) during the study. There were two Alfapump® failures (5%) during the Pioneer Study; one caused by a motor malfunction and one caused by a microprocessor communication error. A significant number of infectious events were detected in Cohort I. After implementing changes to the protocol regarding antibiotic prophylactic measures, a decrease in the incidence of infectious episodes in Cohort 2 was observed.
Patient Perspective	The device may offer some advantages in terms of patient acceptability and quality of life as it would mean less visits to the hospital and would allow patients to travel more. The implantation procedure takes under one hour and is thought to be minimally invasive although it is inserted subcutaneously under general anaesthetic.

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Cost analysis summary	The cost of the entire system including pump device, catheters and programmer is £20,000 plus VAT. This includes lifelong maintenance of the device and free replacement in the event of device failure. The battery in the pump has a life span of two years.
Financial impact PbR: In-tariff	There may be potential cost savings associated with the use of the Alfapump® as the number of hospital admissions for paracentesis will be reduced. The PbR tariff for paracentesis is £749 (combined day case / elective tariff HRG FF53A). Therefore based on 24 hospital admissions per annum (based on 2 weekly) the cost of paracentesis is £18,000 per patient per annum compared to an annual cost of approximately £12,000 (including VAT) for the Alfapump® system. A cost-utility analysis model carried out by the manufacturer suggests that the Alfapump® system in comparison with large volume paracentesis (LVP) over a time horizon of 9 months had lower cost (£26 798 and £39 702 respectively) and produced more benefits (0.87 QALYs and 0.67 QALYs respectively). It is expected that 5 patients per annum will be suitable for the Alfapump® system across the NE & C region.