

CentriMag for heart failure

Medtech innovation briefing

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Summary

- The **technology** described in this briefing is CentriMag, a ventricular assist device for short-term cardiopulmonary support in people with heart failure. The smaller version for children is called PediVAS.
- The **innovative aspects** are that it is the only short-term ventricular assist device available for 30-day use and that it operates without mechanical bearings or seals, which may reduce blood-related complications.
- The intended **place in therapy** would be as an alternative to other short-term ventricular assist devices, or in addition to medical therapy in people with end-stage or acute heart failure. It would be used until a person recovers, until they have a heart transplant, or while a decision is being made about suitable longer-term treatments.

- The **key points from the evidence** summarised in this briefing are from 1 systematic review and 5 retrospective case series, 3 of which were set in the UK. These studies included 1,060 patients with pre- or post-cardiotomy cardiogenic shock, graft failure or rejection after transplant, or right ventricular failure after left ventricular assist device placement. Results show that CentriMag can be used in different groups of people with heart failure with varying survival rates. Device failure was rare (0.08% to 0.58% of cases) but adverse events occurred. There was a higher incidence of bleeding and thrombosis in children than in adults.
- **Key uncertainties** around the evidence are that there is a lack of comparative evidence and so the benefits of CentriMag in children or adults compared with alternative treatments, such as extracorporeal membrane oxygenation, are not clear.
- The **cost** of CentriMag is £6,042 per unit (exclusive of VAT). The **resource impact** would be in addition to standard care because of increased staffing and care needs.

The technology

CentriMag is an external blood pump, connected to a surgically inserted cannula. It is designed for short-term cardiopulmonary support (up to 30 days) in adults and children with end-stage or acute heart failure. It can be used to support a person until they recover (bridge to recovery), until they have a heart transplant (bridge to transplant), or while a decision is being made about suitable longer-term treatments (bridge to decision). The device can provide total circulatory support (acting as a biventricular assist device, or BiVAD) or individual left or right ventricular support (LVAD or RVAD). It can also be used as a part of an extracorporeal membrane oxygenation (ECMO) circuit, but this use is beyond the scope of this briefing.

CentriMag comprises a reusable motor, a console, a flow probe and a single-use centrifugal blood pump and circuit. The circuit has an inflow and an outflow cannula, which are both inserted through an cut in the upper abdomen and surgically connected to the heart. These cannulae are then connected to the external pump, which sits in the motor and is connected to the console. A flow probe is used to measure the blood flow. The external parts of CentriMag sit on a trolley, next to the patient. The motor magnetically levitates the impeller (rotor) and operates without mechanical bearings or seals. This minimises friction, wear and heat generation, which may reduce the risk of blood-related complications.

PediVAS (called PediMag in the US) is a smaller version of CentriMag specifically designed for children. It works with the same hardware platform as the CentriMag.

The innovation

CentriMag is the only short-term VAD that is CE marked for 30-day use; other short-term VADs can only be used for up to 7 days. CentriMag is small enough to allow transfer of patients between beds and wards if needed, which could enable patient transfer in emergency situations.

Current NHS pathway

NICE has produced guidelines on [acute heart failure](#) and [chronic heart failure](#), as well as interventional procedures guidance on [short-term circulatory support with LVADs as a bridge to cardiac transplantation or recovery](#), and [implanting an LVAD for destination therapy in people ineligible for heart transplantation](#).

Management for end-stage or acute heart failure currently involves medical therapy, mechanical assist devices, such as intra-aortic balloon pumping or LVADs, and heart transplant. If a mechanical assist device is needed, treatment would take place at a specialist cardiothoracic transplant or ECMO centre.

Implantable LVADs are most commonly used to support a patient's haemodynamic function for months or years while they await a heart transplant, although they may also be used as indefinite long-term support in people ineligible for heart transplant. Short-term LVADs are used to support a person's haemodynamic function as they recover from a heart attack or other cardiac event. Long-term VADs can be used for short-term support, but their prohibitive prices mean that this is rarely considered in practice. Most VAD support in the NHS is for the left ventricle; RVADs are limited to acute graft failure after heart transplants. Occasionally BiVAD implantation is needed when implanting an LVAD reveals right ventricular failure.

Patients who may need temporary haemodynamic support include those who:

- have had cardiac surgery
- have had an acute heart attack

- have deteriorating end-stage heart failure
- have had a heart transplant
- have right ventricular failure after LVAD implantation.

Temporary haemodynamic support may also be used in people with cardiogenic shock. Around 2% to 5% of all patients having cardiac surgery experience cardiogenic shock afterwards ([Shuhaiber, 2008](#)). About 4% of people hospitalised with a heart attack develop acute cardiogenic shock, and around 40% of these die ([Goldberg, 2016](#)).

NICE is unaware of any other devices which are CE marked for 30 days' use.

Population, setting and intended user

CentriMag is used in NHS cardiothoracic transplant and ECMO centres. It is used by cardiac surgeons, intensivists and cardiologists.

Adopting CentriMag is unlikely to need any significant changes to current NHS care pathways in centres that already do transplants and extracorporeal membrane oxygenation.

Costs

Device costs

The list price for CentriMag is £6,042 (converted from €6,710 on 2 November 2016). Including capital equipment costs, maintenance costs and single-use elements, the cost per use is estimated to be £3,542 for CentriMag and £3,559 for PediVAS ([Borisenko, 2014b](#)).

Costs of standard care

The manufacturer sponsored a cost impact study of short-term VADs and extracorporeal life-support systems which evaluated 3 indications: children and adults with post-cardiac surgery cardiogenic shock, children and adults with deteriorating end-stage heart failure, and adults only with post-acute myocardial infarction cardiogenic shock. The analysis only included device costs, placement costs and the cost of replacement procedures. Three

devices were compared in adults (CentriMag, Biomedicus BPX-80 [off-label use], and Abiomed Impella) and 2 were compared in children (PediVAS and Biomedicus BPX-50 [off-label use]).

Across all indications, in both adults and children, CentriMag and PediVAS cost less than the comparator (which the authors stated were available and used in the NHS). For example, in adults with end-stage heart failure, the modelled device costs for CentriMag, BPX 80/BPX 50 (with Carmeda) and Impella 5.0 were £15,669, £35,731 and £74,865 respectively. However, the analyses provide only a limited basis for comparing CentriMag with current standard care for several reasons:

- Costs for some likely comparators, such as extracorporeal membrane oxygenation, intra-aortic balloon pump or intensive medical support, were not included.
- Some of the comparisons included off-label device use.
- The analysis only included costs that differed across devices; any costs that were the same were not included. Costs will therefore be higher in practice than those presented because the estimates did not include the costs of ICU and other supportive care.
- Comparator devices are not directly comparable with CentriMag because they are licensed for shorter use times (2 to 5 days). The analysis therefore included costs for continued replacement of these devices until the average time for support was met.

Resource consequences

According to the manufacturer, use of CentriMag is well established within the NHS.

Adoption of the technology would be as an alternative to ECMO support. It could be used instead of or in addition to intensive inotropic support or intra-aortic balloon pumps in the appropriate indications.

NHS England currently commissions long-term VADs for bridging to transplantation for use within designated transplant centres. However, CentriMag could be used in cardiac centres that are currently not transplant centres, in particular for the post-cardiotomy indication. If used in other cardiac centres, it could increase the number of patients for whom CentriMag could be used. If this led to improved survival, it may increase demand for medications, VAD and heart transplant provision, as well as hospital stays. People

having CentriMag would need recovery time in post-cardiac surgery beds, and this use would have staffing and training implications.

Regulatory information

CentriMag was CE marked as a class IIb device in 2002. PediVAS was CE marked as a class IIb device in 2007.

A search of the Medicines and Healthcare Products Regulatory Agency website revealed that no manufacturer Field Safety Notices or Medical Device Alerts have been issued for this technology.

Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

No equality issues were identified.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the published process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

This briefing includes a summary of 1 systematic review and 5 studies that were published

after the systematic review was done, including a total of 1,060 patients.

The systematic review ([Borisenko, 2014a](#)) included 38 studies (678 patients in total), most of which were retrospective case series. The 5 other studies ([Hashmi, 2015](#); [Loforte, 2014](#); [Mohite, 2014](#); [Sabashnikov, 2013](#); [Takayama, 2014](#)) were all retrospective case series and included a total of 382 patients. The evidence suggests that CentriMag or PediVAS can be used in different patient groups with heart failure, resulting in varying survival rates. These groups include patients with pre- or post-cardiotomy cardiogenic shock, graft failure or rejection after transplant, and right ventricular failure after LVAD placement. However, there is no evidence comparing CentriMag with other interventions. Adverse events were also seen, with a higher incidence of bleeding and thrombosis in children than adults. Device failure was rare.

Table 1 summarises the clinical evidence as well as its strengths and limitations.

Strengths and limitations of the evidence

Because the evidence is mostly retrospective and based on case series without a comparator, it is of low quality and inherently prone to bias. Some of the series include consecutive patients, but in others specific groups or types of patients were selected with little or no explicit criteria reported. For this reason it is difficult to ascertain how representative these populations are to an NHS setting, despite some of the studies being done in the UK. There may also be some overlap across studies in the patients included.

Few studies were done in children, and when they were separate analyses were not possible. Some patients were supported for longer than 30 days, and in most studies there was little description of the intervention or other supportive treatments used during the study. Results from studies that analysed data from over several years may not be applicable to current practice because of changes in patient management. Most of the studies included outcomes of success rates and survival, but there was little evidence on the levels of anticoagulant drug use or micro-emboli formation, which are outcomes stated by the manufacturer to be relevant to this device.

Table 1: Summary of clinical evidence

Study size, design and location	Intervention	Outcomes	Strengths and limitations
<p><u>Borisenko et al. 2014a</u></p> <p>Systematic review and meta-analysis of 38 studies (case series/cohort studies) with 678 patients</p> <p>Argentina, Austria, Croatia, Czech Republic, Germany, Italy, Netherlands, Poland, UK, US</p>	<p>Magnetically levitated centrifugal pump; CentriMag or PediVAS (manufactured by Levitronix or Thoratec), for extracorporeal membrane oxygenation (excluded from briefing) or ventricular assistance.</p>	<p>CentriMag can be used in different patient groups, including pre-cardiotomy, post-cardiac surgery cardiogenic shock, post-transplant graft failure or rejection, post-LVAD placement right ventricular failure.</p> <p>Survival rates and adverse event rates were reported; however comparative data were not identified.</p>	<p>Limited by the quality of included studies, (majority were retrospective case series) and small number of studies for each indication.</p> <p>Includes 2 studies where the mean duration of support was more than 30 days.</p> <p>Presents an overall summary of study quality but not for individual studies.</p> <p>Statistical heterogeneity between studies not reported, but appears to be present on inspection of the forest plots.</p> <p>Sponsored by the CentriMag manufacturer.</p>

<p><u>Loforte et al. 2014</u> Retrospective case series with 50 patients Two centres Italy</p>	<p>Levitronix CentriMag. Surgical placement reported to be traditional (reference provided) and anticoagulant protocols proposed by the manufacturer adopted. No further details.</p> <p>Mean support time 10.2 (SD 6.6) days (range: 3 to 43 days).</p> <p>LVAD: n=12 RVAD: n=24 BiVAD: n=14. No comparator.</p>	<p>The CentriMag led to successful outcomes for approximately half of those supported with refractory heart failure. Adverse events during the period of support were low, although deaths occurred in approximately one third of patients.</p>	<p>Retrospective case series, unclear if cases were consecutive or any missing.</p> <p>CentriMag used during period of 2004 to December 2012 (9 years) and there may have been changes in patient management over this time frame which will not be accounted for in the study results.</p> <p>Some inconsistencies in results between text and tables.</p> <p>Unclear if representative population, few characteristics reported.</p> <p>No conflicts of interest from authors.</p>
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<p><u>Mohite et al. 2014</u> Retrospective case series with 31 patients (of 154 total implanted) Single centre UK</p>	<p>CentriMag, mean duration of support 11.7 days (range 0-65). 17 (54.8%) supported for > 7 days, of which 3 (9.7%) supported for > 30 days. LVAD 64.5%, RVAS 9.7%, BiVAD 28.8% Anticoagulation protocols, target flow, and monitoring of patients described. No comparator.</p>	<p>CentriMag can be used for patients with post-cardiotomy cardiogenic shock as a bridge to decision. Over half of patients died on support.</p>	<p>Limited to post-cardiotomy cardiogenic shock indication. Retrospective study of prospectively collected data. Focus of paper is on comparison between survivors and non-survivors and risk factors for surviving. Study period from 2004 to 2011. There may have been changes in patient management over this time frame which will not be accounted for in the study results. No conflicts of interest from authors.</p>
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<p><u>Takayama et al. 2014</u> Retrospective case series with 143 patients (158 device implants) Single centre US</p>	<p>CentriMag. Median duration of support: 14 days (IQR, 8–26). 158 device runs in 143 patients: BiVAD 66.5%, RVAD 26.0%, LVAD 7.5% Anticoagulant protocols described. No comparator.</p>	<p>Bridge to decision therapy with surgical CentriMag VAD is feasible in a variety of refractory cardiogenic shock settings, with a third to up to three quarters of patients surviving to discharge. Neurologic complications occurred in 7-17% of patients.</p>	<p>Retrospective case series, although states that cases were consecutive. CentriMag used during period of 2007 to 2012 and there may have been changes in patient management over this time frame which will not be accounted for in the study results. Some patients received devices on more than one occasion. Rates presented for type of device (e.g. LVAD, BiVAD) were based on number of device runs rather than number of participants. 2 authors received consultant fees from Thoratec.</p>
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<p><u>Hashmi et al. 2015</u> Retrospective case series with 33 patients Single centre UK</p>	<p>CentriMag. Median duration of support 26 days (2-110). No comparator.</p>	<p>A third of patients died on support but over half of patients were alive at 10 years.</p>	<p>Published as conference abstract only, limited details reported. Retrospective case series, although states consecutive cases. CentriMag used during period of 2005 to 2014 and there may have been changes in patient management over this time frame which will not be accounted for in the study results. Range of support duration was over the 30 days indication (up to 110 days). Includes 2 patients having ECMO.</p>
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<p><u>Sabashnikov et al. 2013</u> Retrospective case series with 125 patients Single centre UK</p>	<p>CentriMag as bridge to recovery, long-term VAD or transplantation. No comparator.</p>	<p>Around a third to two thirds of the different patient groups were weaned from support; the remaining patients died on support.</p>	<p>Published as a conference abstract only, limited details reported. Retrospective case series, although states that cases were consecutive. Updated data from a subgroup of these patients are reported in <u>Mohite, 2014</u>. CentriMag used during period of 2003 to 2011 and there may have been changes in patient management over this time frame which will not be accounted for in the study results. Some patients had devices more than once. Some proportions were based on number of devices rather than number of participants.</p>
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Recent and ongoing studies

No ongoing or in-development trials were identified.

Specialist commentator comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Three specialist commentators currently use CentriMag or PediVAS regularly. Two others are familiar with the technology but have not used it.

Level of innovation

The specialist commentators felt that the basic principle of CentriMag is well established in other devices, but most said that the device represents a significant variant; 1 stated that this is the only magnetically levitated temporary centrifugal blood pump available. All of the commentators agreed that special training is needed to use CentriMag.

Potential patient impact

Three specialist commentators stated that patients with the potential for myocardial recovery are likely to benefit from CentriMag, particularly after myocardial infarction or for people with acute cardiomyopathy. One specialist commentator stated that CentriMag may also benefit people whose cardiac function has been reduced to a life-threatening extent. One specialist commentator felt that there is currently limited high quality evidence to support a clear patient benefit and that CentriMag should be introduced only as part of research exploring the clinical and cost benefits.

CentriMag may help to stabilise patients before a heart transplant. Two specialist commentators noted that some patients would not have survived without CentriMag. One specialist commentator felt that CentriMag may reduce the number of repeat procedures needed for patients by being a bridge between short- and long-term devices.

Potential system impact

The specialist commentators noted that using CentriMag needs a highly skilled and specialised team in an intensive care environment, and that more intensive care beds would be needed. Increased patient survival could lead to a rise in inpatient stay, increased outpatient visits, and an increased demand for donor organs and medications.

Three of the commentators expressed concerns about the use of CentriMag outside existing cardiac transplant and ECMO centres. One noted the significant training needed, and that the complexity of managing these patients means that they should only be treated in specialist centres familiar with extracorporeal support. The commentators felt that there should be a mandatory registry for patients using CentriMag in order to capture data on patient outcomes. Another commentator noted that the staff resources and facilities needed to use CentriMag were only possible at designated transplant centres. A third commentator stated that special training is needed to use CentriMag and that the technology would need to be used regularly enough to gain expertise and maintain competence. However, 1 commentator disagreed, saying that in the UK there is a need for non-transplant cardiothoracic surgical units to provide short-term haemodynamic support before transfer to a transplant centre. This would relieve pressure on the ITU resources of transplant centres, while providing support to patients with cardiogenic shock, who could recover or be suitable for transplant or longer-term support. Another commentator added that an important use of CentriMag is in the cardiothoracic surgical unit for post-cardiotomy salvage.

One specialist commentator thought that using CentriMag could lead to cost savings for the NHS, but the others thought this was unlikely. One stated that CentriMag may be less preferable to ECMO because inserting a VAD requires cardiac surgery, whereas ECMO is relatively easy and has lower costs.

General comments

One specialist commentator stated that current medical management has a high mortality rate.

One specialist commentator was concerned that there is growing enthusiasm among clinicians to use temporary cardiac support, despite limited clinical evidence of patient benefit and substantial associated costs. They also felt that there was limited expertise in its use outside existing ECMO and transplant centres. Another felt that being able to offer temporary mechanical circulatory support should be the standard of care for any hospital providing a cardiac surgical service, either in the form of ECMO or temporary VADs, but that there is no evidence as to which approach or device is better.

One specialist commentator noted that CentriMag may allow people with cardiogenic shock after acute heart attack to recover consciousness earlier, which would allow assessments of brain function to be made.

Specialist commentators

The following clinicians contributed to this briefing:

- Dr Nick Barrett, Consultant in Critical Care, Guy's and St Thomas' NHS Foundation Trust. No conflicts of interest declared.
- Dr Farzin Fath-Ordoubadi, Consultant Cardiologist, Central Manchester University Hospitals NHS Foundation Trust. No conflicts of interest declared.
- Dr Guy MacGowan, Consultant Cardiologist, the Newcastle upon Tyne Hospitals NHS Foundation Trust. No conflicts of interest declared.
- Mr Andrew Parry, Consultant Congenital Cardiac Surgeon, University Hospitals Bristol NHS Foundation Trust. No conflicts of interest declared.
- Mr Steven Tsui, Consultant Cardiothoracic Surgeon & Director of Transplant Service, Papworth Hospital NHS Foundation Trust. No conflicts of interest declared.

Representatives from the following patient organisations were contacted during the production of this briefing:

- British Heart Foundation.
- British Cardiac Patients Association.

Development of this briefing

This briefing was developed for NICE by Birmingham and Brunel Consortium. The [interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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