NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

SCOPE

Spectra Optia Apheresis System for automated red blood cell exchange in patients with sickle cell disease

1 Technology

1.1 Description of the technology

The Spectra Optia Apheresis System (Terumo) is used for automated red blood cell depletion and exchange in adults or children with sickle cell disease who are on a long term or temporary/medium-term transfusion regime.

The system comprises 3 components: the apheresis machine; embedded software; and a single-use disposable blood tubing set. Venous access for the Spectra Optia Apheresis System is usually through an arm or large leg vein. The latter is a more complicated procedure that requires additional expertise, often involving vascular radiologists. Following removal of blood from the patient, the constituent components are separated by the Spectra Optia Apheresis System using continuous flow and centrifugation. A patented optical detection technology (known as automated interface management) monitors the position and thickness of the blood components and feeds this information to the selected device protocol which can adjust appropriate pumps and valves in real time to efficiently remove targeted components. The device protocol, software and automated interface management system facilitates replacing the removed fractions with donor red blood cells and fluid as required. The procedure typically takes 2–3 hours.

The Spectra Optia Apheresis System should be operated by trained healthcare professionals. The system may be used in a specialist day-care setting and, if the patient is well enough, they may return to normal activities immediately after the procedure.

1.2 Regulatory status

The Spectra Optia Apheresis System has a CE mark as a class IIb medical device for the design, development and manufacture of blood cell separators. It first received a CE mark in 2007.

The device may also be used to perform mononuclear cell collection, collection of donor lymphocytes and haematopoietic progenitor cells, white blood cell depletion, bone marrow processing, platelet depletion, polymorphonuclear cell (including granulocyte) collections and plasma exchange. These uses are outside the scope of this evaluation.

1.3 Claimed benefits

The benefits to patients claimed by the company are:

- Automated red blood cell exchange using the Spectra Optia Apheresis System has a longer clinical effect than manual red blood cell exchange meaning that patients would require treatment only every 6–8 weeks in comparison with every 3–4 weeks.
- Automated red blood cell exchange with this device is faster than manual red blood cell exchange with treatment lasting approximately 2–3 hours in comparison to 4–8 hours. This makes the procedure more convenient for patients which may improve compliance.
- Treatment with the Spectra Optia Apheresis System could allow patients to reduce or cease iron chelation treatment due to reduced iron overloading. This medication can cause significant side effects which may lead to poor compliance.
- Increased patient compliance and efficiency of automated red blood cell exchange, in comparison with other transfusion methods could improve disease outcomes for patients. These improved outcomes include: reduced

incidence of stroke, reduced frequency and severity of pain crises, reduced incidence of acute chest syndrome, improved outcomes following surgery, and increased body mass index and growth in paediatric patients as well as improved general quality of life.

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

- The Spectra Optia Apheresis System maintains haematocrit levels which prevents iron overloading. This allows for the reduction or cessation of treatment (within 12–18 months, depending on the severity of iron overloading) with high cost, infusion-pump administered iron chelator desferrioxamine or oral chelators such as deferasirox and deferiprone.
- Reduced hospital stay and staff time are needed as automated red blood cell exchange can be performed by a trained nurse, is faster (2–3 hours for 6–8units), and allows for an increased interval between treatments (every 6–8 weeks). During manual red blood cell exchange, doctors are required to estimate haematocrit levels so that each unit of blood drawn off is replaced by the correct volume of packed red blood cells. This procedure can last for between 6 hours (3–4 units exchanged) and 2 days (8 units exchanged) depending on the patient's sickle haemoglobin (HbS) levels. Manual red blood cell exchange should be repeated every 3–4 weeks.
- Reduced complications from sickle cell disease leading to reduced hospitalisations and associated treatment.
- The depletion-exchange protocol of the machine makes better use of donor blood as only the required fraction is used allowing the remaining blood components to be used in other patients.

1.4 Relevant diseases and conditions

Patients with sickle cell disease have a mutated variant of haemoglobin that causes red blood cells to form a distinctive sickle shape. These red blood cells do not flow easily and can cause blockages, known as vaso-occlusive crises. This can occur in any part of the body but is most serious when it restricts the blood flow to major organ systems.

While serious organ damage is a concern, all vaso-occlusive events are extremely painful for the patient and will often require emergency admission to hospital and pain management with opiates. These acute episodes of extreme pain are likely to have a negative impact on the person's work or school and daily life. More serious complications such as stroke and acute chest syndrome can lead to significant morbidity and a reduced life expectancy.

In England, there are an estimated 240,000 carriers of the sickle cell trait and around 13,500 people with sickle cell disease. Sickle cell disease is the most common serious genetic disorder in England and affects 1 in 2000 live births, or 350 babies a year. People with sickle cell disease tend to live in urban areas where birth prevalence may be as high as 1 in 300. However, the NHS Sickle Cell & Thalassaemia Screening Programme has identified affected infants in all parts of the country. Sickle cell disease is most common in people whose families originate from Africa, the Caribbean, the Eastern Mediterranean, the Middle East and Asia. In the UK the majority of people with sickle cell disease are of African and Caribbean descent. In this population, at least 1 in 10–40 people carry the sickle cell trait and 1 in 60–200 has sickle cell disease. Around 10–20% of patients with sickle cell disease require regular blood transfusions or red blood cell exchange.

1.5 Current management

The most commonly available current management involves replacing sickled red blood cells with healthy red blood cells or drug therapy or a combination of both, with the aim of lessening symptoms and long-term complications. The type of treatment delivered depends on the severity of symptoms and will always be planned in order to minimise the risk of further complications. The range of treatment is similar for adults and children with sickle cell disease although the order in which they are given may vary. Both adults and children with sickle cell disease are more susceptible to infections and antibiotic prophylaxis and immunisations are routinely recommended for children who are not contra-indicated. NICE has produced a guideline on the management of an acute painful sickle cell episode in hospital. NHS Sickle Cell and

Thalassemia Screening Programme has also produced Sickle cell disease in childhood, standards and guidelines for clinical care.

The chemotherapy drug hydroxycarbamide may be prescribed since it stimulates the production of fetal haemoglobin which is unaffected by the sickle cell mutation. However, this drug may be ineffective in up to 25% of patients, often causes serious side effects and cannot be taken by either men or women prior to conception or by women during pregnancy or breastfeeding. If hydroxycarbamide is ineffective, contra-indicated or associated with side effects, the patient may require a long-term red blood cell transfusion regime.

Automated or manual red blood cell exchange in sickle cell disease is used in the treatment of acute sickle cell complications or to prevent long-term complications by reducing the proportion of sickle cell haemoglobin (HbS) cells in circulation. For example, patients with sickle cell disease may require red cell exchange for stroke prevention (most commonly used in children with sickle cell disease who are identified as being at a high risk of stroke after transcranial Doppler investigations), established or threatened organ failure and acute chest syndrome. A temporary blood transfusion regime may be set up for patients with leg ulcers or for those discontinuing hydroxycarbamide prior to conception or pregnancy.

If donor red blood cells are given in a blood transfusion, the haematocrit (percentage of the volume of whole blood that is made up of red blood cells) may increase above 30% which increases the risk of hyperviscosity and vaso-occlusive events. Increased haematocrit levels can also lead to iron overload, which can lead to important clinical consequences. As there is no mechanism for the body to remove the extra iron from transfused red blood cells it accumulates in the liver, heart and other organs. If left untreated this excess iron can cause organ damage, liver and heart failure, along with type II diabetes. Iron overloading is a complex clinical problem which is very difficult to treat. Iron chelation therapy is used to treat iron overload but these drugs

can cause unpleasant side effects and may need to be administered via an overnight infusion pump.

Red blood cell exchange, automated or manual, can produce a significant reduction in HbS (target usually <30%) thereby reducing the risk of hyperviscosity or iron overload. Venous access can be problematic in patients requiring regular or recurrent treatment.

Manual red blood cell exchange involves removing whole blood and infusing the patient intravenously with donor red cells, to replace the sickle cells. This method is time-consuming and it may not be possible to achieve the desired reduction in HbS% in one procedure. It is usual that 3-4 units of blood will be necessary, with the exchange of each unit lasting 2-4 hours. This treatment needs to be repeated every 3-4 weeks. It should also be noted that managing iron overloading during manual red blood cell exchange is very difficult and usually requires the patient to be on chelation therapy. Chelation therapy is administered orally or through an infusion pump and causes significant side effects such as hepatic dysfunction, gastrointestinal disturbance, fever, headache and injection site reactions. The severity of these side effects may lead to low compliance in some patients leading to more serious iron-overload complications such as an increased risk of heart failure, liver or spleen enlargement and death due to toxicity.

All transfusion therapies for patients with sickle cell anaemia carry a risk of alloimmunisation which occurs in approximately 18% of patients and may result in them not being able to receive certain types of blood. Alloimmunisation is common as the majority of donor red blood cells in the UK come from white Europeans.

2 Reasons for developing guidance on the Spectra Optia Apheresis System for sickle cell disease

The Committee considered that Spectra Optia may offer benefits to some patients with sickle cell disease through an improvement in morbidity and clinical outcomes. These benefits include a possible reduced length of treatment, increased treatment interval, improved control of sickle cell concentration and reduced iron overload, in comparison with manual red blood cell exchanges and top-up transfusions.

The Committee considered that the replacement of manual red blood cell exchange with Spectra Optia could result in cost savings for the healthcare system arising from a reduced need for iron chelation therapy.

The Committee noted that development of medical technology guidance on this device, if it is positive, may help promote wider adoption and better access for patients.

3 Statement of the decision problem

	Draft scope issued by NICE
Population	Sickle cell disease patients requiring a medium or long-term exchange transfusion regime.
Intervention	Spectra Optia Apheresis System
Comparator(s)	Manual red blood cell exchange
Outcomes	The outcome measures to consider include: Primary outcomes • Percentage of total haemoglobin that is HbS (HbS%), relative to target percentage (usually <30%) • Duration of exchange procedure • Frequency of treatment • Patient haematocrit (measure relative to prescribed target for therapy) • Iron overload and requirement for chelation therapy • Clinical outcomes including frequency of stroke, multi-organ failure, acute chest syndrome and pain crises • Quality of life • Length of hospital stay • Staff time and staff group/grade • Frequency of top-up transfusion required to treat sickle cell complications Secondary outcomes • Ease of venous access, bruising and haematoma • Device-related adverse events • Hospital admissions • Donor blood usage • BMI and growth in children
Cost analysis	Comparator(s): Manual red blood cell exchange Costs will be considered from an NHS and personal social services perspective. The time horizon for the cost analysis will be sufficiently long to reflect any differences in costs and consequences between the technologies being compared. Sensitivity analysis will be undertaken to address uncertainties in the model parameters, which will include scenarios in which different numbers and combinations of devices are needed.
Subgroups to be considered	• Children and adults at high risk of stroke • Pregnant or breastfeeding women • Patients with iron overload • Patients with acute chest syndrome • Patients with multi-organ failure • Children
Special	Sickle cell disease can have a substantial and long-term adverse

<table>
<tr><td>considerations, including those related to equality</td><td colspan="2">effect on the ability to carry out normal day-to-day activities, and as such many people with sickle cell disease will be considered to be disabled, a protected characteristic under the Equality Act, 2010.
Some religious groups, for example Jehovah's Witnesses, are opposed to blood transfusions. Religion and belief is a protected characteristic under the Equality Act, 2010.
The majority of people with sickle cell disease in the UK are of black African or Caribbean family origin.
There is currently an inequity of access to the highest standards of care for sickle cell disease as treatments are only available in certain cities in the UK.</td></tr>
<tr><td rowspan="5">Special considerations, specifically related to equality issues</td><td colspan="2"></td></tr>
<tr><td>Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristics?</td><td>No</td></tr>
<tr><td>Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?</td><td>No</td></tr>
<tr><td>Is there anything specific that needs to be done now to ensure MTAC will have relevant information to consider equality issues when developing guidance?</td><td>No</td></tr>
<tr><td colspan="2">Delete as appropriate, if yes please provide further details here:</td></tr>
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4 Related NICE guidance

Published

- Sickle cell acute painful episode: Management of an acute painful sickle cell episode in hospital. NICE clinical guideline 143 (2012). Available from www.nice.org.uk/guidance/CG143
- Antenatal care. NICE clinical guideline 62 (2008). Available from www.nice.org.uk/guidance/CG62

Under development

NICE is developing the following guidance (details available from www.nice.org.uk):

- There is no related guidance under development.

5 External organisations

5.1 Professional organisations

5.1.1 Professional organisations contacted for expert advice

At the selection stage, the following societies were contacted for expert clinical and technical advice:

- British Society of Haematology
- Clinical Reference Group for Haemoglobinopathy
- Royal College of Pathologists
- Rare Disease UK
- UK Forum on Haemoglobin Disorders

5.1.2 Professional organisations invited to comment on the draft scope

The following societies have been alerted to the availability of the draft scope for comment:

- Rare Disease UK
- Royal College of Pathologists
- The British Society for Haematology
- UK Forum on Haemoglobin Disorders

5.2 Patient organisations

At the selection stage, NICE's Public Involvement Programme contacted the following organisations for patient commentary and alerted them to the availability of the draft scope for comment:

- Action for Sick Children
- African Caribbean Leukaemia Trust
- Bliss
- Different Strokes
- Ethnic Health Foundation
- National Childbirth Trust
- Sickle Cell and Young Stroke Survivors
- Sickle Cell Society
- Specialised Healthcare Alliance
- Stroke Association
- Together for Short Lives
- Tommy's