NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

Review decision

Review of MTG28: Spectra Optia for automatic red blood cell exchange in patients with sickle cell disease

This guidance was issued in March 2016.

1. Recommendation

The guidance remains valid and should therefore be designated as static guidance. Literature searches are carried out every 5 years to check whether any of the medical technologies guidance on the static list should be flagged for review.

GE may wish to consider amending the title of the guidance and section 1.1 and 1.4 to 'people with sickle cell disease' to bring it in line with NICE's person-centric writing style. We also suggest combining recommendations 1.1 and 1.2 for simplicity. This could be processed by the digital editors as a post-publication change.

2. Original objective of guidance

To assess the case for adoption of Spectra Optia for automated red blood cell exchange in adults and children with sickle cell disease.

3. Current guidance

1.1 The case for adopting Spectra Optia for automated red blood cell exchange in patients with sickle cell disease is supported by the evidence. Spectra Optia is faster to use and needs to be done less often than manual red blood cell exchange.

1.2 Spectra Optia should be considered for automated red blood cell exchange in patients with sickle cell disease who need regular transfusion.

1.3 NICE recommends collaborative data collection to generate further clinical evidence on some outcomes of treatment with Spectra Optia. In particular, there is a need for long-term data on how automated and manual exchange affect iron overload status and the subsequent need for chelation therapy.

1.4 Based on current evidence and expert advice on the anticipated benefits of the technology when used in patients with iron overload, cost modelling shows that

in most cases using Spectra Optia is cost saving compared with manual red blood cell exchange or top-up transfusion. The savings depend on the iron overload status of the patient, and are more likely to be achieved if devices already owned by the NHS can be used to treat sickle cell disease. The estimated cost saving for adopting Spectra Optia is £18,100 per patient per year, which has the potential to save the NHS in England £12.9 million each year.

4. Rationale

There has been an increase in the use of the technology to treat sickle cell disease, the clinical experts noted that the guidance had helped achieve this. The clinical experts stated that increased use of Spectra Optia has led to better clinical outcomes for patients, reduced use of iron chelation therapy, reduced number of blood packs required and improved availability meaning that patients did not have to travel as far for treatment.

Fifteen new full papers and 24 abstracts were identified in the literature search. The EAC reviewed the new evidence and concluded that although the evidence base had increased in size, it had not improved in quality. The new evidence supported the conclusions of the original assessment report and did not provide any new information that would change the recommendations. The EAC noted that this might have been expected as the original guidance noted (section 3.17) the limitations in study methodologies are due to a lack of clinical equipoise between Spectra Optia and manual red blood cell exchange (in favour of Spectra Optia).

During the initial review stage, the company informed NICE that there have been no changes to the technology and the price of the technology had not changed. The EAC identified 2 new economic studies but these did not provide new information. The cost of deferasirox appears to have increased due to changes in the tablet dose available according to the BNF. As the cost of iron chelation therapy was one of the main drivers of cost savings in the model this could increase the cost savings gained by using Spectra Optia. No other significant changes in costs were identified and there is no evidence for the long-term cost benefits of using Spectra Optia.

5. New evidence

The search strategy from the original assessment report was re-run. References from June 2015 onwards were reviewed. Additional searches of clinical trials registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the care pathways. The company was asked to submit all new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked indication for use for their technology. The results of the literature search are discussed in the ‘Summary of

evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

5.1 Technology availability and changes

There have been no changes to the technology, model performance, mode of action, or CE marking status of the technology.

5.2 Clinical practice

There are no NICE clinical guidelines on red blood cell exchange. Existing NICE guidance on managing sickle cell disease addresses patients with an acute painful episode, which is outside the scope of this evaluation.

The national programme of Haemoglobin Disorders Reviews, conducted by the West Midlands Quality Review Service, published quality standards in 2018 stating that all patients on long-term transfusions should have access to automated exchange transfusion and that protocols and audits for its use should be in place. These quality standards were originally developed separately for children and adults' services, to support the Sickle Cell Society guidelines, published in 2008 as noted in the original assessment report, now updated in 2018. This includes the following recommendations concerning transfusions in adults and children with sickle cell disease:

- All hospitals that admit sickle cell disease patients should have protocols and training in transfusion for sickle cell disease including manual exchange procedures.
- Automated exchange transfusion should be available to all patients with sickle cell disease and should be provided by specialist centres.
- Specialist centres should audit their use of blood transfusion in the acute and chronic setting to ensure its use is consistent with national guidance.

5.3 NICE facilitated research

None

5.4 New studies

The updated literature search by the EAC identified 15 full papers in peer reviewed journals and 24 abstracts. The full papers included 3 comparative studies (Escobar et al 2017, Fasano et al 2016, Woods et al 2017), 3 technical studies (Buyukkurt et al 2018, Kim et al, 2016, Poullin et al, 2016), 6

single armed studies (Ballas and Lyon 2016, Joshua Daniel et al 2016, Tsitsikas et al 2017b, Tsitsikas et al 2016, Hequet et al 2019, Myers et al 2016) and 2 economic studies (Dedeken et al 2018, Tsitsikas et al 2017a). There were 6 abstracts for comparative studies, the remaining 18 were classified as 'other'.

In the comparative studies, Spectra Optia was compared with manual red blood cell exchange in 7 studies, with partial red blood cell exchange in one study and with both partial red blood cell exchange and simple top up transfusion in another study. The EAC noted that these studies lacked experimental design descriptions and were likely to be subject to a high degree of confounding and bias. The study findings support the recommendations and conclusions of the published guidance but do not address any uncertainties of the original evidence base.

The 3 technical studies reported that the performance of Spectra Optia was broadly equivalent to its predecessor, Cobe Spectra. These findings agree with the conclusions of the original assessment report.

5.5 Cost update

As there were no changes to the cost of the technology the cost model was not updated. The EAC did not identify any new evidence that would change the assumptions used in the cost modelling. The cost of deferasirox appears to have increased due to changes in the tablet dose available according to the BNF. As the cost of iron chelation therapy was one of the main drivers of cost savings in the model this could increase the cost savings gained by using Spectra Optia (e.g. for a 15 year old taking the maximum dose, this could amount to an additional saving of nearly £6000 per year). No other significant changes in costs were identified and there is no evidence for the long-term cost benefits of using Spectra Optia.

6. Summary of new information and implications for review

The new evidence is unlikely to have a material effect on the recommendations and should be reviewed again in 5 years' time.

7. Implementation

The company and clinical experts noted that there has been increased uptake of Spectra Optia for sickle cell disease since guidance publication. Spectra Optia has been commissioned in several trusts and the therapeutic apheresis service (TAS), based in Birmingham, Bristol, Leeds, Liverpool, London, Manchester, Oxford, and Sheffield. Providers may be reimbursed through Commissioning for Quality and Innovation (CQUIN, B13), although this may not be adequate to recoup all provider

costs (Tsitsikas et al., 2017a). Spectra Optia is increasingly becoming an established treatment in people with SCD. The company have stated that there are 41 NHS users of Spectra Optia.

8. Equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

No equality issues were identified during the original guidance development. It was noted that sickle cell disease is most common in people whose families originate from Africa, the Caribbean, the Eastern Mediterranean, the Middle East and Asia. Race is a protected characteristic under the 2010 Equality Act.

Some people with sickle cell disease may be classed as disabled, disability is a protected characteristic under the 2010 Equality Act.

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 Committee also heard that specialist centres that treat people with sickle cell anaemia with the Spectra Optia apheresis system are concentrated in urban areas and are not equally equipped in terms of the treatments they offer. This means that some people have to travel long distances to receive treatment.

No new equality issues or considerations were identified during the guidance review. Clinical experts stated that improved access to Spectra Optia has meant that some patients do not have to travel as far for treatment.

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Appendix 1 – explanation of options

If the published Medical Technologies Guidance needs updating NICE must select one of the options in the table below:

Options	**Consequences**	**Selected – 'Yes/No'**
Amend the guidance and consult on the review proposal	The guidance is amended but the factual changes proposed have no material effect on the recommendations.	No
Amend the guidance and do not consult on the review proposal	The guidance is amended but the factual changes proposed have no material effect on the recommendations.	No
Standard update of the guidance	A standard update of the Medical Technologies Guidance will be planned into NICE's work programme.	No
Update of the guidance within another piece of NICE guidance	The guidance is updated according to the processes and timetable of that programme.	No

If the published Medical Technologies Guidance does not need updating NICE must select one of the options in the table below:

Options	**Consequences**	**Selected – 'Yes/No'**
Transfer the guidance to the 'static guidance list'	The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Medical Technologies Guidance on the static list should be flagged for review.	Yes
Defer the decision to review the guidance	NICE will reconsider whether a review is necessary at the specified date.	No
Withdraw the guidance	The Medical Technologies Guidance is no longer valid and is withdrawn.	No

Appendix 2 – supporting information

Relevant Institute work

Published

None

In progress

None

Registered and unpublished trials

None

Appendix 3 – changes to guidance

Table 1: proposed amendments to original guidance

Section of MTG	Original MTG	Proposed amendment
Title	Spectra Optia for automatic red blood cell exchange in patients with sickle cell disease	Spectra Optia for automatic red blood cell exchange in people with sickle cell disease
1.1	The case for adopting Spectra Optia for automated red blood cell exchange in patients with sickle cell disease is supported by the evidence. Spectra Optia is faster to use and needs to be done less often than manual red blood cell exchange.	The case for adopting Spectra Optia for automated red blood cell exchange in people with sickle cell disease who need regular transfusions is supported by the evidence. Spectra Optia is faster to use and needs to be done less often than manual red blood cell exchange.
1.2	Spectra Optia should be considered for automated red blood cell exchange in patients with sickle cell disease who need regular transfusion.	
1.4	Based on current evidence and expert advice on the anticipated benefits of the technology when used in patients with iron overload, cost modelling shows that in most cases using Spectra Optia is cost saving compared with manual red blood cell exchange or top-up transfusion. The savings depend on the iron overload status of the patient, and are more likely to be achieved if devices already owned by the NHS can be used to treat sickle cell disease. The estimated cost saving for adopting Spectra Optia is £18,100 per patient per year, which has the potential to save the NHS in England £12.9 million each year.	Based on current evidence and expert advice on the anticipated benefits of the technology when used in people with iron overload, cost modelling shows that in most cases using Spectra Optia is cost saving compared with manual red blood cell exchange or top-up transfusion. The savings depend on the iron overload status of the person being treated, and are more likely to be achieved if devices already owned by the NHS can be used to treat sickle cell disease. The estimated cost saving for adopting Spectra Optia is £18,100 per person per year, which has the potential to save the NHS in England £12.9 million each year.

References

1. Ballas, S. K. & Lyon, D. (2016). Safety and efficacy of blood exchange transfusion for priapism complicating sickle cell disease. Journal of Clinical Apheresis, 31, 5-10.

2. BNF. 2019. British National Fomularly (deferasirox) [Online]. Available: https://bnf.nice.org.uk/medicinal-forms/deferasirox.html [Accessed 23rd January 2020].

3. Buyukkurt, N., Kozanoglu, I. et al. (2018) Comparative efficacy in red blood cell exchange transfusions with different apheresis machines in patients with sickle cell disease. Indian Journal of Hematology and Blood Transfusion, 34, 495-500.

4. Dedeken, L., Phu Quoc, L. E. et al. (2018) Automated RBC exchange compared to manual exchange transfusion for children with sickle cell disease is cost-effective and reduces iron overload. Transfusion, 58, 1356-1362.

5. Escobar, C., Moniz, M., et al. (2017) Partial red blood cell exchange in children and young patients with sickle cell disease: Manual versus automated procedure. Acta Medica Portuguesa, 30, 727-733.

6. Fasano, R. M., Leong, T., et al. (2016) Effectiveness of red blood cell exchange, partial manual exchange, and simple transfusion concurrently with iron chelation therapy in reducing iron overload in chronically transfused sickle cell anemia patients. Transfusion, 56, 1707-15.

7. Hequet, O., Poutrel, S. et al. (2019) Automatic depletion with Spectra Optia allows a safe 16% reduction of red blood cell pack consumption in exchanged sickle cell anemia patients. Transfusion, 59, 1692-1697.

8. Joshua Daniel, M., Muddegowda, P. H. et al. (2016) Study of twenty one cases of red cell exchange in a tertiary care hospital in Southern India. Journal of Clinical and Diagnostic Research, 10, EC28-EC30.

9. Kim, J., Joseph, R. et al. (2016). Comparison of Spectra Optia and COBE Spectra apheresis systems' performances for red blood cell exchange procedures. Transfusion and Apheresis Science, 55, 368-370.

10. Myers, S. N., Eid, R. et al. (2016) Long-term erythrocytapheresis is associated with reduced liver iron concentration in sickle cell disease. J Pediatr Hematol Oncol, 38, 22-6.

11. Sickle Cell Society (2018) Standards for the Clinical Care of Adults with Sickle Cell Disease in the UK [Online]. Available: https://www.sicklecellsociety.org/wp-content/uploads/2018/05/Standards-for-the-Clinical-Care-of-Adults-with-Sickle-Cell-in-the-UK-2018.pdf [Accessed 13th January 2020].

12. Tsitsikas, D. A., Ekong, A. et al. (2017a) A 5-year cost analysis of automated red cell exchange transfusion for the management of recurrent painful crises in adult patients with sickle cell disease. Transfusion and Apheresis Science, 56, 466-469.

13. Tsitsikas, D. A., Orebayo, F. et al. (2017b) Distinct patterns of response to transfusion therapy for different chronic complications of sickle cell disease: A useful insight. Transfusion and Apheresis Science, 56, 713-716.

14. Tsitsikas, D. A., Sirigireddy, B. et al. (2016) Safety, tolerability, and outcomes of regular automated red cell exchange transfusion in the management of sickle cell disease. Journal of Clinical Apheresis, 31, 545-550.

15. Woods, D., Hayashi, R. J. et al. (2017) Increased complications of chronic erythrocytapheresis compared with manual exchange transfusions in children and adolescents with sickle cell disease. Pediatr Blood Cancer, 64(11) doi: 10.1002/pbc.26635.