**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Single Technology Appraisal**

# Voxelotor for treating haemolytic anaemia in people with sickle cell disease [ID1403]

**Final scope**

## Remit/appraisal objective

To appraise the clinical and cost effectiveness of voxelotor within its marketing authorisation for treating haemolytic anaemia in people with sickle cell disease.

## Background

Sickle cell disease is the name given to a group of lifelong inherited conditions that affect haemoglobin. The most common and often severe type of sickle cell disease occurs when people inherit a copy of the beta globin gene with the sickle mutation from both parents (homozygous sickle cell anaemia). Heterozygous sickle cell anaemia occurs when people inherit one copy of the beta globin gene with the sickle mutation from one parent and a different variant of the beta globin gene from the other parent. In all cases, the abnormal haemoglobin, known as haemoglobin S, tends to form polymers (or chains) with other haemoglobin S molecules. These polymers cause red blood cells to become rigid and misshapen, resembling a crescent (or sickle).[1]

Sickle-shaped red blood cells do not last as long in the body as regular shaped round red blood cells and get broken down more readily in a process known as haemolysis.[2] People with sickle cell disease often have anaemia because too much haemolysis occurs and there are not enough red blood cells to carry oxygen throughout the body. Sickle-shaped red blood cells also do not flow easily through blood vessels and bond abnormally with other blood cells and blood vessel walls which can cause blockages.[2] This may lead to insufficient oxygen being delivered to tissues, causing ischaemic injuries and excruciating pain (known as acute sickle cell crises). Chronic complications caused by anaemia and sickle cell crises include progressive organ damage, fatigue and shortness of breath. Acute complications may also include acute chest syndrome and stroke.[1]

It is estimated that there are 15,000 people with sickle cell disease in England.[3] The prevalence of sickle cell disease varies considerably across different ethnic communities, mainly affecting people of African or African-Caribbean family background, although the sickle gene is found in all ethnic groups.[4] The prevalence of the disease is increasing because of immigration into the UK, new births and increased survival.[5]

Sickle cell disease causes significant morbidity and mortality and usually requires lifelong treatment. Management in England focuses on reducing the chances of experiencing a sickle cell crisis by avoiding dehydration, sudden changes in temperature and infection. Sickle cell crises may be extremely painful and will often require emergency admission to hospital and pain management with paracetamol, non-steroidal anti-inflammatory drugs and opiates. Hydroxycarbamide can also be used to increase the production of foetal haemoglobin, which improves blood cell hydration and reduces red blood cell adhesion. This can reduce both acute painful crises and acute chest syndrome (caused by reduced blood flow in the lungs) in people with recurrent painful crises. Blood transfusions including exchange transfusions (where sickle red blood cells are replaced with healthy red blood cells) and simple (top-up) transfusions can help to maintain a healthy proportion of normal red blood cells to sickle red blood cells. Allogenic stem cell transplants may be considered but are not done often because of the significant risks involved.[6]

## The technology

Voxelotor (Oxbryta, Global Blood Therapeutics Inc) is a haemoglobin S allosteric modulator. Voxelotor increases haemoglobin's ability to hold on to more oxygen, which prevents polymerisation and keeps red blood cells in their normal shape, helping to prevent haemolysis and associated anaemia. It is administered orally.

Voxelotor does not currently have marketing authorisation in the UK for any indication. It has been studied in clinical trials compared with placebo in people with sickle cell disease aged 2 years to 65 years and in single-arm open-label studies in people with sickle cell disease aged 4 years and above.

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| **Intervention(s)** | Voxelotor |
| **Population(s)** | People with sickle cell disease |
| **Comparators** | Established clinical management without voxelotor including:<br>• hydroxycarbamide<br>• blood transfusions (exchange and top-ups)<br>• best supportive care. |
| **Outcomes** | The outcome measures to be considered include:<br>• changes to haematological parameters (haemoglobin levels)<br>• number and severity of sickle cell crises<br>• complications arising from sickle cell disease<br>• markers of haemolysis<br>• mortality<br>• adverse effects of treatment<br>• health-related quality of life. |
| **Economic analysis** | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.<br>The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.<br>Costs will be considered from an NHS and Personal Social Services perspective. |

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| **Other considerations** | If the evidence allows, the following subgroups will be considered:<br>• subgroups defined by combination treatment with/without hydroxycarbamide<br>• subgroups defined by genotypes of sickle cell disease<br>Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator. |
| **Related NICE recommendations and NICE Pathways** | **Related Technology Appraisals:**<br>Crizanlizumab for preventing sickle cell crises in sickle cell disease (TA743). November 2021<br>**Medical Technologies guidance:**<br>Spectra Optia for automatic red blood cell exchange in patients with sickle cell disease (MTG28). March 2016<br>**Related Guidelines:**<br>Sickle cell disease: managing acute painful episodes in hospital (2012) NICE clinical guideline 143<br>**Related Quality Standards:**<br>Sickle cell disease (2014) NICE quality standard 58 |
| **Related National Policy** | NHS England Clinical Commissioning Policy: Allogeneic Haematopoietic Stem Cell Transplantation for adults with sickle cell disease 2020<br>NHS England Service Specification: Specialist Haemoglobinopathy Teams Service Specification (all ages) 2019<br>NHS England (2019) Service specification no.18 NHS Sickle Cell and Thalassaemia Screening Programme.<br>Public Health England (2019) NHS Sickle Cell and Thalassaemia Screening Programme Standards<br>The NHS Long Term Plan, 2019. NHS Long Term Plan<br>NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) |

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| | NHS England (2018) Manual for prescribed specialised services 2018/2019. Chapter 114 Specialist haemoglobinopathy services (adults and children) p.307<br><br>Public Health England (2018) Sickle cell and thalassaemia: screening handbook<br><br>NHS England (2017) BI3 Automated Exchange Transfusion for Sickle Cell Care QIPP 16-17 S28-B&I PSS CQUIN Scheme<br><br>Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017<br><br>NHS England (2016) Clinical Commissioning Policy: Treatment of iron overload for transfused and non transfused patients with chronic inherited anaemias Ref: 16070/P<br><br>Public Health England (2015) Sickle cell and thalassaemia screening: community outreach good practice<br><br>NHS England (2013) 2013/14 NHS standard contract for specialised services for haemoglobinopathy care (All ages) Ref: B08/S/a |

## References


1. Nevitt SJ, Jones AP, Howard J. Hydroxyurea (hydroxycarbamide) for sickle cell disease. Cochrane Database of Systematic Reviews 2017, Issue 4
2. Kato et al. 2018; Sickle cell disease, Nature Reviews Disease Primers; 4, 18010
3. NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) (Accessed June 2021)
4. Clinical Knowledge (2016) Sickle cell disease: prevalence (Accessed June 2021)
5. NHS sickle cell and thalassaemia (SCT) screening programme (Accessed June 2021)
6. NHS, Sickle cell disease: treatment (Accessed June 2021)