NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Voxelotor for treating sickle cell disease ID1403

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of voxelotor within its marketing authorisation for treating 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 flow easily through the blood vessels and can cause blockages. This may lead to insufficient oxygen being delivered to tissues, causing ischaemic injuries and excruciating pain (known as acute sickle cell crises). Other acute and chronic complications including organ damage acute chest syndrome and stroke.[1] The risk of stroke is highest in children between the ages of 2 and 16. 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. 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.

It is estimated that there are 15,000 people with sickle cell disease in England.[2] The prevalence of sickle cell disease varies considerably across different ethnic communities, mainly affecting people of African or African-Caribbean origin, although the sickle gene is found in all ethnic groups.[3] The prevalence of the disease is increasing because of immigration into the UK, new births and increased survival.[4]

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 also be considered in children who have severe disease which does not respond to hydroxycarbamide.

The technology

Voxelotor (GBT440, 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. 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.

Intervention(s)	Voxelotor
Population(s)	People with sickle cell disease
Comparators	Established clinical management without voxelotor including: • hydroxycarbamide • blood transfusions (exchange and top-ups) • allogeneic stem cell transplants • best supportive care • crizanlizumab (subject to ongoing NICE appraisal).

Outcomes	The outcome measures to be considered include: • changes to haematological parameters (haemoglobin levels) • number and severity of sickle cell crises • complications arising from vaso-occlusive crises (including stroke, acute chest syndrome, organ damage) • mortality • adverse effects of treatment • 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. 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. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	If the evidence allows, the following subgroups will be considered: • subgroups defined by combination treatment with/without hydroxycarbamide • subgroups defined by genotypes of sickle cell disease 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 Medical Technologies guidance:** Spectra Optia for automatic red blood cell exchange in patients with sickle cell disease (MTG28). March 2016 **Related Guidelines:** Sickle cell disease: managing acute painful episodes in hospital (2012) NICE clinical guideline 143 **Related Quality Standards:** Sickle cell disease (2014) NICE quality standard 58

	Related NICE Pathways: Sickle cell disease: acute painful episode (2012, updated 2018) NICE pathway
Related National Policy	NHS England Clinical Commissioning Policy: Allogeneic Haematopoietic Stem Cell Transplantation for adults with sickle cell disease 2020 NHS England Service Specification: Specialist Haemoglobinopathy Teams Service Specification (all ages) 2019 NHS England (2019) Service specification no.18 NHS Sickle Cell and Thalassaemia Screening Programme. Public Health England (2019) NHS Sickle Cell and Thalassaemia Screening Programme Standards The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) NHS England (2018) Manual for prescribed specialised services 2018/2019. Chapter 114 Specialist haemoglobinopathy services (adults and children) p.307 Public Health England (2018) Sickle cell and thalassaemia: screening handbook NHS England (2017) BI3 Automated Exchange Transfusion for Sickle Cell Care QIPP 16-17 S28-B&I PSS CQUIN Scheme 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 NHS England (2016) Clinical Commissioning Policy: Treatment of iron overload for transfused and non transfused patients with chronic inherited anaemias Ref: 16070/P Public Health England (2015) Sickle cell and thalassaemia screening: community outreach good practice

	NHS England (2013) 2013/14 NHS standard contract for specialised services for haemoglobinopathy care (All ages) Ref: B08/S/a

Questions for consultation

Have all relevant comparators for voxelotor been included in the scope?

Which sickle cell genotypes were included in the trial / are likely to be included in the marketing authorisation?

Which treatments are considered to be established clinical practice in the NHS for treating sickle cell disease?

How should best supportive care be defined?

At what point in the treatment pathway would allogenic stem cell transplant be used? Is it a relevant comparator?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations' appropriate?

Are there any other subgroups of people in whom voxelotor is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider voxelotor will fit into the existing NICE pathway, sickle cell disease: acute painful episode?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which voxelotor will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider voxelotor to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of voxelotor can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Nevitt SJ, Jones AP, Howard J. Hydroxyurea (hydroxycarbamide) for sickle cell disease. Cochrane Database of Systematic Reviews 2017, Issue 4 (Accessed June 2020)
2. NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) (Accessed June 2020)
3. Clinical Knowledge (2016) Sickle cell disease: prevalence (Accessed June 2020)
4. NHS sickle cell and thalassaemia (SCT) screening programme (Accessed June 2020)