Medicines & Healthcare products Regulatory Agency

MHRA

Early Access to Medicines Scientific Opinion - Public Assessment Report	
Product	**Voxelotor**
EAMS indication	**Voxelotor is indicated for the treatment of hemolytic anemia in adult and pediatric patients 12 years and older with sickle cell disease (SCD). Voxelotor can be administered alone or in combination with hydroxycarbamide.**
Company	**GBT UK Limited**
EAMS number	**54981/0001**
EAMS Scientific Opinion date	**25 January 2022**

Introduction
The aim of the Early Access to Medicines Scheme (EAMS) is to provide earlier availability of promising new unlicensed medicines and medicines used outside their licence, to UK patients that have a high unmet clinical need. The MHRA scientific opinion provides benefit and risk information to physicians who may wish to prescribe the EAMS medicine under their own responsibility. More information about the scheme can be found here:
http://www.mhra.gov.uk/Howweregulate/Innovation/EarlyaccesstomedicinesschemeEAMS/index.htm

The scientific opinion is based on assessment of the information supplied to the MHRA on the benefits and risks of the medicine. As such this is a scientific opinion and should not be regarded as a medicine licensed by the MHRA or a future commitment by the MHRA to license such a medicine. The General Medical Council's guidance on prescribing unlicensed medicines can be found here:
https://www.gmc-uk.org/ethical-guidance/ethical-hub/trans-healthcare#prescribing

What is Voxelotor?
Voxelotor is an orally administered hemoglobin S (HgbS) polymerization inhibitor which binds with a 1:1 stoichiometry and exhibits preferential partitioning to red blood cells (RBCs). By increasing the affinity of Hb for oxygen, voxelotor demonstrated dose-dependent inhibition of HbS polymerization.

This process increases the affinity of HbS for oxygen. As the proportion of oxyhaemoglobin in RBCs increases, Voxelotor prevents the RBC from sickling and improves RBC deformity leading to the decrease of haemolysis and improvement of anaemia in sickle cell disease (SCD).

What is Voxelotor used to treat?
Voxelotor is indicated for the treatment of haemolytic anaemia (haemoglobin ≤ 10.5 g/dL) in adults and paediatric patients 12 years of age and older with SCD. Voxelotor can be administered alone or in combination with hydroxycarbamide.

How is Voxelotor used?
Treatment with voxelotor should be initiated by physicians who have experience in the management of patients with sickle cell disease. The recommended dose of voxelotor is 1,500 mg (three 500 mg tablets) taken orally once daily.

Voxelotor tablets should be swallowed whole with water. Voxelotor can be taken with or without food. Tablets should not be cut, crushed, or chewed because of the unpleasant taste.

If a dose is missed, treatment should be continued on the day following the missed dose. The recommended dose of voxelotor in patients 12 to < 18 years of age is the same as for adults. The safety and efficacy of voxelotor in paediatric patients below the age of 12 years have not been established yet.

How does Voxelotor work?
Patients with sickle cell disease have red blood cells that are shaped like a crescent moon or sickle. Sickle cells cannot carry oxygen as well as healthy red blood cells and do not live as long. This leads to a disorder called sickle cell anaemia. Voxelotor works on a protein in red blood cells called haemoglobin to interfere with the process that causes red blood cells to sickle. Voxelotor helps haemoglobin to do its work, that is, helping red blood cells deliver oxygen throughout the body.

How has Voxelotor been studied?
Voxelotor has been studied in clinical trials of more than 800 subjects with sickle cell disease in 25 studies. The main study involved 274 randomised patients with sickle cell disease and compared voxelotor with a placebo. The main measurement of efficacy was the improvement in blood haemoglobin levels after 24 weeks of treatment.

When should Voxelotor not be given?
Voxelotor is not recommended for children under 12 years due to insufficient data in this age group and should not be given to patients who are allergic to voxelotor or any of the other ingredients of this medicine.

What are the benefits and risks of Voxelotor?

Benefits
There is an unmet need in significant proportion of patients with sickle cell disease who do not respond adequately to currently available treatments or in whom these treatments cannot be administered due to intolerability. The observed improvement in blood haemoglobin levels after treatment with voxelotor therefore offers a significant benefit in the management of patients with sickle cell disease.

Risks
The majority of the reported side effects were non-serious and included diarrhoea, product dose omission, nausea, headache and abdominal pain.

Why has Voxelotor been given a positive Early Access to Medicine Scientific opinion?
Current treatment options for sickle cell disease (SCD) are limited to the drugs that target recurrent vaso-occlusive crises (hydroxyurea, crizanlizumab), blood transfusions (on-demand or prophylactic) and erythropoietin (not licensed for the treatment of sickle cell disease.

Additionally, symptomatic treatments, such as antibiotics, ACE-inhibitors, analgesics are being used to control the disease symptoms. The only curative treatment option is hematopoietic stem cell transplantation which is mainly reserved for severe forms.

For the treatment of haemolytic anaemia associated with SCD, there is not specific treatment in Europe. Therefore, there is an unmet need in a significant proportion of patients who do not respond adequately to currently available treatments or in whom these treatments cannot be administered due to intolerability.

What are the uncertainties?
Data are still limited regarding the long-term effectiveness or risks of voxelotor. The company that makes voxelotor (Global Blood Therapeutics) will provide additional information when it becomes available.

Are there on-going clinical studies?
Studies with voxelotor are on-going in adult and paediatric patients to collect long-term safety and effectiveness data.

What measures are in place to monitor and manage risks?
A risk management plan has been developed to ensure that voxelotor is used as safely as possible. Information will be collected about patients before they enter the scheme. Healthcare professionals will be asked by the company to report side effects experienced by patients receiving voxelotor through the scheme, as well as medication errors, overdose, and pregnancies. They will receive comprehensive training on adverse events reporting including the form to be used prior to commencement of patient treatment. Safety data will be reviewed and reported to the MHRA on a regular basis by the company.

Other information about voxelotor – see EAMS Treatment Protocol