Content of this Plain Language Summary

The objective of the Plain Language Summary is to help the general public understand EUnetHTA assessments. You can find the link to the full assessment report later in the summary.

What is included in this Plain Language Summary? First, this document explains what EUnetHTA is and what this network does. Second, you will find the summary of the assessment.

What is EUnetHTA?

EUnetHTA is the European Network for Health Technology Assessment (HTA). EUnetHTA was established to create an effective and sustainable network for HTA across Europe. Our partners work together to help develop information to contribute to HTA in European countries. For more information on our goals and how we work, please visit our website and our patient flyer.

EUnetHTA consists of over 80 partners that are all non-profit organisations. All partner organisations either produce or support the production of HTA reports. For more information on HTA, visit EUnetHTA's Frequently Asked Questions.

EUnetHTA does not give any advice on reimbursement of a specific health technology. The reimbursement decision is a national or regional decision. This means that reimbursement of health technologies can also differ between countries in Europe.

What does EUnetHTA do?

EUnetHTA supports national and regional research institutions and health ministries in their decision-making. For this task, EUnetHTA uses specific methods to assess health technologies. Health technologies that may be assessed by EUnetHTA include medicines and other health technologies such as specialist medical care, surgical interventions and diagnostic tests. The purpose of this plain language summary is to help the general public understand the findings from this assessment.

Summary of the assessment

This section provides a summary of the assessment and was published on 25/11/2020. To get a better understanding of commonly used HTA concepts, we advise you to look at the HTAi glossary.

Why did we conduct this assessment?

The purpose of this EUnetHTA assessment is to give national healthcare systems robust information about the therapy under assessment.

What is the context of this assessment?

Sickle cell disease is a group of inherited health conditions. Sickle cell disease changes the shape and function of red blood cells. Instead of the normally oval-shaped blood cells, the blood cells of sickle cell disease patients become sickle shaped. These abnormal red blood cells can cause problems, because they are stiff and can block small blood vessels (vaso-occlusion). The blockage of blood vessels in bones, lungs, or any organ in the body can result in extremely painful events, because oxygen cannot reach the organs. These episodes of severe pain are called vaso-occlusive crises (abbreviation: VOCs). Sickle-shaped red blood cells also do not live as long as healthy blood cells. Therefore, people have low levels of red blood cells, causing anaemia, making them tired and weak. Normally, people with sickle cell disease die younger than healthy people (between 40 and 60 years old). Sickle cell disease is more common among people from Africa, the Caribbean, the Middle East, Eastern Mediterranean and Asia.

There is no medicine that can cure sickle cell disease. The only way people can be cured from sickle cell disease is via stem cell transplantation. However, only few people can receive such a treatment, because a healthy donor needs to be found who matches with the patient. Current treatments aim to relieve pain and try to prevent complications, such as the blockage of blood vessels. The only available approved medication to reduce the frequency of VOCs is hydroxyurea. However, not all people are able to take this medicine. This is due to: side effects, another (health) condition that does not allow the use of the medicine, or because the effects of the medicine cannot be checked regularly.

Recently, a treatment called crizanlizumab has been granted a conditional European Marketing Authorisation in November 2020. It is a treatment that is given via an infuse in the blood veins and the dosage is 5 milligrams per kilogram body weight. Crizanlizumab is developed to prevent blood cells in the bloodstream from sticking together and blocking blood vessels. This should reduce the number and the severity of the VOCs, which are common in people with sickle cell disease.

What did EUnetHTA review?

Through this assessment, EUnetHTA reviewed how well crizanlizumab works and how safe it is in patients with sickle cell disease. This is compared to what is currently used to treat these patients.

What is the drug under review?	Crizanlizumab
What is the study group?	People with sickle cell disease aged 16 years and older with recurrent vaso-occlusive crises
What is the drug compared to?	Best supportive care with or without hydroxyurea

What are the outcomes this review investigates?	Outcomes on effectiveness of the drug:
	• Mortality
	• Quality of life
	• Number of vaso-occlusive crises per year
	• Number of days in the hospital per year
	• Time to first vaso-occlusive crisis
	
	Outcomes on safety and side effects of the drug:
	• Adverse events, i.e., any negative medical occurrences that happen during treatment. In particular, adverse events that are:
	  ○ Fatal, life-threating, result in disability
	  ○ Lead to a patient stopping treatment

What are the main findings?

One study on crizanlizumab was relevant for this assessment. This study was found via a systematic search of the literature available up till July 2020. A total of 198 participants with sickle cell disease from the United States, Brazil, and Jamaica were included in this 1-year study. The participants were on average 30 years old (ranging from 16 to 63 years) and 55% was female. Almost all participants were Black (92%).

The study showed that participants treated with crizanlizumab had on average 1.6 vaso-occlusive crises (VOCs) per year. Participants that were treated with "fake" crizanlizumab, a so-called placebo, experienced on average 3.0 VOCs per year.

However, the calculation of these results were questioned. Therefore, the results were re-calculated in another, more appropriate way. These new calculations did not show a difference in the number of VOCs per year between the people that were treated with crizanlizumab or with placebo. Because of this, there is less trust that crizanlizumab helps to prevent VOCs.

Participants who already used hydroxyurea and now also received crizanlizumab had a smaller reduction in the number of VOCs compared to participants who did not use hydroxyurea before the use of crizanlizumab. However, as this was based on a low number of people, it was not possible to draw a strong conclusion.

The study showed that for participants who received crizanlizumab it took longer before they had their first VOC. No improvements were seen in the quality of life of the participants and the number of days in the hospital per year.

Participants that received crizanlizumab did not have more side-effects.

Because the study only lasted for 1 year, there were no results for long-term outcomes, such as death or severe complications related to sickle cell disease.

Did EUnetHTA involve stakeholders?

EUnetHTA values involvement of stakeholders in their assessments. It helps to include patients' experiences and thereby improves the usefulness of the assessments. For this assessment, patient organisations were invited to provide input via an online survey in the beginning of this assessment. The input from patient organisations was used to help make the selection of outcomes that were investigated in this assessment.

Additional information

The Joint Assessment report was written by HTA organisations from the Netherlands (ZIN) and Spain (AEMPS). Organizations from the United Kingdom (NICE), France (HAS) and Slovenia (JAZMP) have contributed in reviewing roles. The full scientific content is reported in EUnetHTA assessment PTJA10 and can be found here. EUnetHTA has received funding from the European Union's Health Programme (2014-2020). The content of this summary reflects the views of the authoring team. This cannot be considered to reflect the views of the entire EUnetHTA or any body of the European Union. Individuals involved in this assessment were cleared for any potential conflict of interests.

If you have further questions, please contact: eunethta@zinl.nl.