Evelina London

NHS
Guy's and St Thomas'
NHS Foundation Trust

Hydroxycarbamide for children with sickle cell disease (SCD)

Information for families

showing we care

What is hydroxycarbamide (also known as hydroxyurea)?

Hydroxycarbamide is a medicine taken by mouth as a liquid or in a capsule or as a tablet (Siklos®). It causes changes in the blood to reduce the frequency and severity of painful episodes, chest complications and the need for blood transfusions in patients with sickle cell disease. It is also thought to prolong life expectancy if taken over a long period of time.

Who is hydroxycarbamide recommended for?

Hydroxycarbamide is often recommended for any patient with sickle cell disease, particularly HbSS SCD. However, hydroxycarbamide is also suggested if your child is experiencing any of the following:

- frequent painful episodes affecting their quality of life
- has had one or more episodes of acute chest syndrome
- they are no longer tolerating blood transfusion programme or they have had no further brain changes on their MRI after being on transfusion for at least a year with normal TCD
- any other complications related to sickle cell disease

Hydroxycarbamide can protect many organs of the body such as kidney or spleen from ongoing damage so is also now being offered to all children with HbSS or HbS/ β^0thalassaemia over the age of 9 months, who may not

have experienced any severe complications of sickle cell disease.

How does hydroxycarbamide work?

In sickle cell disease normal round red blood cells turn into long narrow cells called sickle cells.

The long narrow red blood cells are sticky and cannot move easily through blood vessels, meaning the vessel can easily become blocked.

This blockage causes pain and damage to other parts of the body such as the lungs, kidneys and liver.

All babies are born with a special type of haemoglobin in their red blood cells called fetal haemoglobin (HbF). Haemoglobin carries oxygen around the body.

During the first six months of life the production of fetal haemoglobin decreases and the sickle haemoglobin increases.

Red cells which contain high levels of sickle haemoglobin will turn into sickle red cells.

Fetal haemoglobin helps red blood cells stay round and flexible, allowing them to travel more freely in the blood stream and reducing the clumping/blockages that result in sickle cell crises.

A high fetal haemoglobin protects the red blood cells from turning into sickle cells.

Hydroxycarbamide raises the amount of fetal haemoglobin in red blood cells, thereby reducing sickling. Hydroxycarbamide also reduces the severity of sickle cell disease by:

- Increasing the time that red blood cells survive in the body, which in turn reduces the anaemia (low haemoglobin).
- Reducing the number of white blood cells, especially the cells called neutrophils. Neutrophils are important in fighting infection in the body, but the high neutrophil counts seen in people with sickle cell disease can cause inflammation and trigger sickle cell crises and other complications.
- Reducing the number of blood cells involved in clotting (platelets).

How is it taken?

Hydroxycarbamide is taken by mouth once a day. It is available in liquid, tablet or capsule form. It is usually started at the lower end of the dose range calculated from your child's weight and then gradually increased depending on how they respond, their blood test results, and their growth over time.

Some children notice an improvement on a low dose, but others need a higher dose to benefit. The dose is adjusted gradually and blood tests are checked regularly. Once settled on an effective dose the time interval between blood tests usually gets longer so that they are only necessary every 2 to 3 months. Blood tests are usually checked 2 to 3 weeks after starting or adjusting the dose of Hydroxyurea.

What are the benefits?

Hydroxycarbamide is effective in more than eight in 10 of people who take it.

Definite benefits include:

- reduced number of episodes of severe pain
- reduced severity of pain
- reduced number of attacks of acute chest syndrome
- overall reduction in the need for blood transfusions and admissions to hospital over time
- it can be used as an alternative to regular blood transfusions in some patients who are at increased risk of stroke
- improvement in wellbeing.

Possible benefits:

- prevention of damage to spleen, kidneys and other organs if taken from an early age
- reduction of damage to blood vessels in the brain.

When will your child notice improvement?

Children often feel better quite quickly but it can take about three months before there is any clinical improvement eg reduction in pain. It is recommended that your child takes it for a trial period of at least six months to get an idea of how it is working and for the doctor to know the optimal dose.

Hydroxycarbamide will not work if only taken every now and again. It is not a painkiller, so taking a dose will not produce immediate effects. It does not replace the need to take regular Penicillin V.

Research information

Multicentre study of hydroxycarbamide in sickle cell anaemia

A large collaborative study involving 21 different sites in the US and Canada treated sickle cell patients with either placebo or hydroxycarbamide. Patients taking hydroxycarbamide experienced:

- fewer crises
- longer durations between crises
- fewer acute chest crises
- less need for blood transfusion

The effects of hydroxycarbamide were so beneficial that the study was terminated early and all patients were given hydroxycarbamide *(Charache et al., 1995; New England Journal of Medicine)*.

Comparisons have been made after 10 years and 17.5 years between people with sickle cell disease taking the drug and those who do not. More people who took hydroxycarbamide were alive at the end of the 10 and 17.5 years than those who did not *(Steinberg et al., 2010; American Journal of Hematology).*

BABY HUG study

The BABY HUG study (The Lancet, 2011) found that children between the ages of one and three years with sickle cell anemia receiving hydroxycarbamide had less pain, fewer hospital stays, fewer acute chest crises and less need for blood transfusion than children who did not receive hydroxycarbamide**.**

Side effects and risks

Side effects are not that common but include:

Rashes. Some people notice a faint skin rash or darkening of the skin and nails. This is not harmful and goes away when the hydroxycarbamide is stopped.

Sickness and nausea. Occasionally people feel sick or unwell when taking hydroxycarbamide. This is not usually a severe problem.

Blood count (FBC). Hydroxycarbamide reduces the blood cells produced by the bone marrow, which is a helpful in SCD, but if they go too low the medicine has to be stopped temporarily to allow them to increase again. If the white blood cells (neutrophils) get too low, there is an increased risk of infection, and the medicine has to be stopped and adjusted to allow the count to increase again. If the platelets go too low, this could lead to unusual bruising or bleeding and the need to stop the Hydroxycarbamide temporarily. It is important that your child has regular blood tests for this reason, and will usually be checked 2 to 3 weeks after any dose increase, or starting hydroxycarbamide for the first time.

Pregnancy. For women, it is advisable not to get pregnant whilst taking hydroxycarbamide and the recommendation is to stop taking the medicine three months before planning a pregnancy. The same advice applies to men who are taking it. There is a small amount of evidence that it can affect the quality of sperm, however, sickle cell disease itself can reduce the sperm count. Currently the advice to teenage boys is to provide a sperm sample that can be stored for future use should there be difficulty in fathering a child.

Long-term side effects

Hydroxycarbamide is a form of mild chemotherapy and the beneficial effects in SCD are a result of its action on the bone marrow. We all have a low risk of developing leukaemia or other cancer during our lifetime and some forms of chemotherapy seem to increase that risk. There is no evidence that hydroxycarbamide itself can cause leukaemia or other cancers in patients in SCD and we now have information from over 20 years of use. There is, however, a theoretical risk of damage to the bone marrow if taken over long periods of time.

Fertility: In post-pubertal male patients it has been suggested that hydroxycarbamide has the potential to decrease sperm counts. These normally recover after stopping hydroxycarbamide. It is currently unclear about the effect on pre-pubertal boys. Males on hydroxycarbamide can be offered sperm cryopreservation above the age of 14 years, usually completed when they are 17 -18 years of age.

What is hydroxycarbamide NOT used to treat?

Hydroxycarbamide may not reduce the frequency of, or prevent, sickle cell complications related to:

- leg ulcers
- avascular necrosis (sickle cell related damage to the bones of the hip or shoulder)
- it is not usually used if your child is at increased risk of stroke in the first instance, but may be prescribed at a later date.

Are there any alternatives?

Hydroxycarbamide is currently the best option for modifying the severity of SCD in most patients. Alternatives exist but they are more experimental and more difficult to take. We are happy to discuss this with you.

What should I do now?

If you are interested in giving your child hydroxycarbamide, speak to your consultant or you can discuss it with another member of the sickle cell team.

Taking an unlicensed medicine

Siklos® (hydroxycarbamide tablets) is the only hydroxycarbamide product that is licensed in the UK for the treatment of SCD. Other hydroxycarbamide products are available in the UK for the treatment of other conditions and although they are not licensed for SCD they may be more appropriate for your child.
For more information on unlicensed medicines, please ask your doctor, nurse or pharmacist for a copy of our leaflet **Unlicensed medicines – a guide for patients**.

Alternatively, you can call the Evelina London Medicines Helpline – contact details are at the end of this leaflet.

Contact us

Lead consultant for haemoglobin disorders, and consultant in haematology, **phone:** 020 7188 6203 (secretary), **email:** Dudhma.Banu@gstt.nhs.uk

Lead nurse, **phone:** 020 7188 9432 or 07918 338730 **email:** HaemoglobinopathyCNS@gstt.nhs.uk

Nurse specialist, **phone:** 07771 345847 or 07517 592436 **email:** HaemoglobinopathyCNS@gstt.nhs.uk

Research nurse, **phone:** 020 7188 6637 or 07517 592436

Specialist nurse – community, **phone:** 020 3049 5993 or 07880 781545

Therapy and psychology team, **phone:** 020 7188 9125 or 07817 905844

Help and advice will always be available if you have any questions or concerns. Out of hours, please call the hospital switchboard, **phone:** 020 7188 7188 and ask them to bleep the haematology registrar.

If you need to come to emergency department (A&E) at St Thomas' Hospital, please telephone the department before you arrive, **phone:** 020 7188 2111 and let them know about you child's condition. This will help to improve your child's care when you arrive.

Further information

The Sickle Cell Society, provides advice, information and support to people with SCD and their families, and raises funds for the education of carers and health professionals, **phone:** 020 8961 7795 **website:** www.sicklecellsociety.org

ERIC, education and resources for improving Childhood continence. This charity provides support and help through their website and helpline, **website:** www.eric.org.uk

Evelina London Medicines Helpline
If you have any questions or concerns about your child's medicines, please speak to the staff caring for them or contact our helpline.
phone: 020 7188 3003, Monday to Friday, 10am to 5pm
email: letstalkmedicines@gstt.nhs.uk

Your comments and concerns
For advice, support or to raise a concern, contact our Patient Advice and Liaison Service (PALS), **phone** 020 7188 8801 **email** pals@gstt.nhs.uk. To make a complaint contact the resolution department **phone** 020 7188 3514 **email** complaints2@gstt.nhs.uk

Language and accessible support services
If you need an interpreter or information about your care in a different language or format, please contact the department your appointment is with

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