South Thames Sickle Cell & Thalassaemia Network

A guide to hydroxycarbamide (Hydroxyurea)

This information sheet is intended to help answer questions you may have about taking hydroxycarbamide for the management of sickle cell disease.

What is hydroxycarbamide (also known as Hydroxycarbamide)?

Hydroxycarbamide is a medicine taken by mouth. It causes changes in the blood to reduce the frequency 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

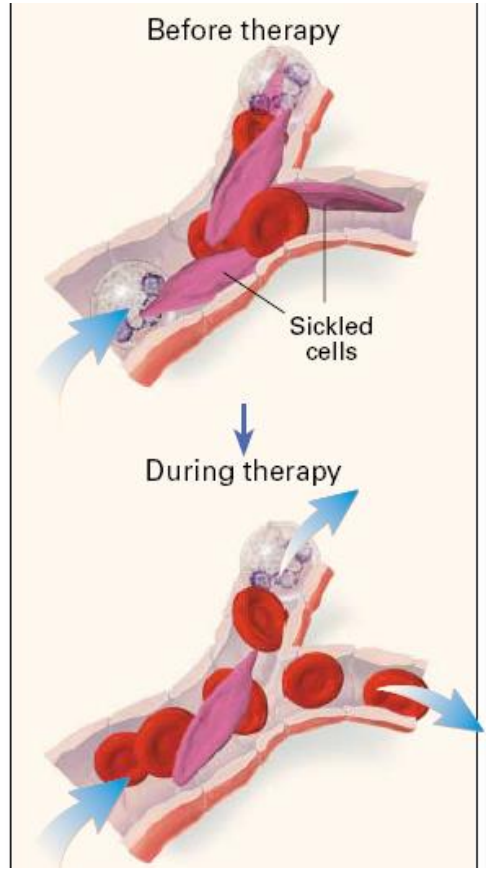
Who is hydroxycarbamide recommended for?

Hydroxycarbamide is often recommended if your child is experiencing frequent painful episodes affecting their quality of life, and/or has had one or more episodes of acute chest syndrome. Because hydroxycarbamide can protect many organs of the body from ongoing damage it 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?

- Red cells contain Haemoglobin which carries oxygen around the body.

- 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.

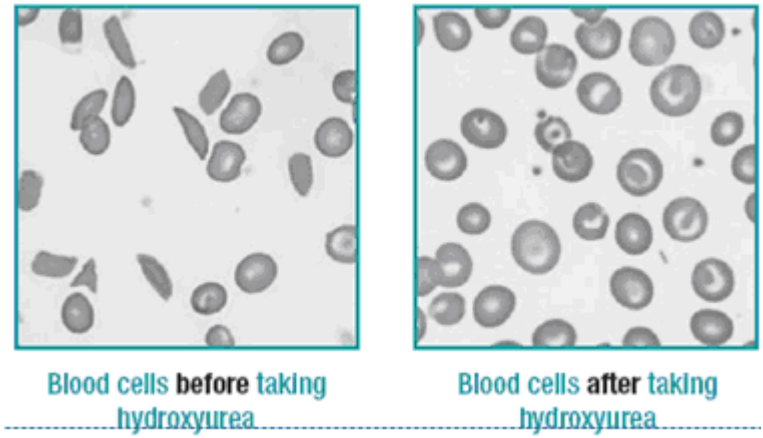
- This blockage causes pain and damage to other parts of the body such as the lungs, kidneys and liver.

- When born babies have mostly fetal haemoglobin (HbF), the levels of this falls over the 1st 6 months of life as they produce increasing amounts of adult haemoglobin (HbA) whereas babies with sickle cell disease produce increasing amounts of sickle haemoglobin (HbS).

- 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 life span of sickle cells in the body, which in turn reduces the anaemia (low haemoglobin)
- reducing the number of white blood cells called neutrophils, which are important in fighting infection in the body, but the high neutrophil counts seen in people with sickle cell disease

are associated with inflammation and trigger sickle cell crises and other complications.

- reducing the number of platelets, which are often increased in sickle cell patients and makes their blood stickier.
- It has additional effects on blood vessels and blood flow all resulting in reduced risk of complications.

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 a standard dose based on your child's weight and adjusted according to their response and blood test results.

The dose will increase as your child's weight increases with age.

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 2-3 months.

What are the benefits?

Hydroxycarbamide is effective in more than 80% of people who take it.

Definite benefits:

- 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

- Reduction in 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 well being Possible benefits:
- Reduction of damage to blood vessels in the brain
- Prevention of damage to kidneys and other organs if taken from an early age

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 6 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.***

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 Haematology).*

BABY HUG study

The BABY HUG study (The Lancet, 2011) found that children between the ages of 1 and 3 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.

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What have patients said about hydroxycarbamide?

"Once I got over the idea of having to have yet another medication it did a lot of good for me. It reduced the amount of time I spent in hospital. Before I took it I was in hospital 3-5 times a year. Since taking it in the last year I have only been in 2 times. The gaps are a lot bigger now. I used to have lots of small crises in between which I'd cope with at home, but these are much rarer now. I've also felt a lot healthier in myself. I can breathe better, move better and my joints feel better". NA, male age 28

"Hydroxycarbamide has been life changing for me. Prior to taking it I spent a lot of time in hospital; as much as 6 months of the year. Since taking it this has stopped. The frequency of my crises has reduced dramatically and so has the intensity. I used to have crises that were excruciatingly painful, but now they're a lot more manageable. So, it really has been life changing, it's made a massive difference"

Side effects and risks

What are the side effects of hydroxycarbamide?

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 Hydroxycarbamide reduces the white cell count in the blood. This is probably a good thing but if the white cells get too low, there is an increased risk of infection and the medicine must be stopped to allow the count to increase again. It is important that your child has regular blood tests for this reason.
- Pregnancy. For women it is important not to get pregnant whilst taking hydroxycarbamide and the advice is to stop taking the medicine 3 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 affects

- The beneficial effects of Hydroxycarbamide 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 medication may increase that risk.
- However, there is no evidence that Hydroxycarbamide itself can cause leukaemia or other cancers in patients with SCD and we now have safety information for over 30 years.
- There is, however, a theoretical risk of damage to the bone marrow if taken over long periods of time.

Are there any alternatives?

Hydroxycarbamide is currently the best option for modifying the severity of SCD in most patients. Alternatives exist including blood transfusions and other more experimental options. We are happy to discuss these with you in clinic. Bone Marrow (Stem Cell) Transplantation is currently the only cure for SCD.

Contact details:

If you have any questions or concerns about your medicines, please speak to the staff caring for you.

Your comments and concerns

For advice, support or to raise a concern, contact our Patient Advice and Liaison Service (PALS). To make a complaint, contact the complaints department at your sickle centre.

Language and Accessible support services

If you need an interpreter or information about your care in a different language or format, please get in touch with language support at your sickle centre

NHS 111

Offers medical help and advice from fully trained advisers supported by experienced nurses and paramedics. Available over the phone 24 hours a day. t: 111

NHS Choices – Provides online information and guidance on all aspects of health and healthcare, to help you make choices about your health w: www.nhs.uk

Additional contacts can be found on the STSTN website (www.ststn.co.uk)

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