

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?

Hydroxycarbamide is a medicine in a capsule that you take by mouth. It causes changes in the blood to reduce the frequency of sickle cell crises and the need for blood transfusions in patients with sickle cell disease. It is also sometimes known as hydroxyurea.

Who is hydroxycarbamide recommended for?

Hydroxycarbamide is often recommended if you one or more of the following things apply to you.

- You have moderately severe or severe sickle cell disease.
- You have had three or more acute hospital admissions for sickle cell crisis in the last 12 months.
- You have experienced acute sickle chest syndrome and needed a blood transfusion or admission to the high dependency unit.
- You have had a stroke and are no longer tolerating an exchange blood transfusion programme.
- You have any other complications related to sickle cell disease.

The recommendations of the authors of the BABY HUG trial (published in *The Lancet*, 2011) were that all children with sickle cell anaemia are considered for treatment with hydroxycarbamide from a young age due to its impact in reducing the severity of SCD. This recommendation is made irrespective of the level of severity of their SCD.

Acknowledgements

Vanderbilt University Medical Centre, Children's Hospital. (2012) "Family Guide to Hydroxyurea Therapy". Excerpts used with permission.

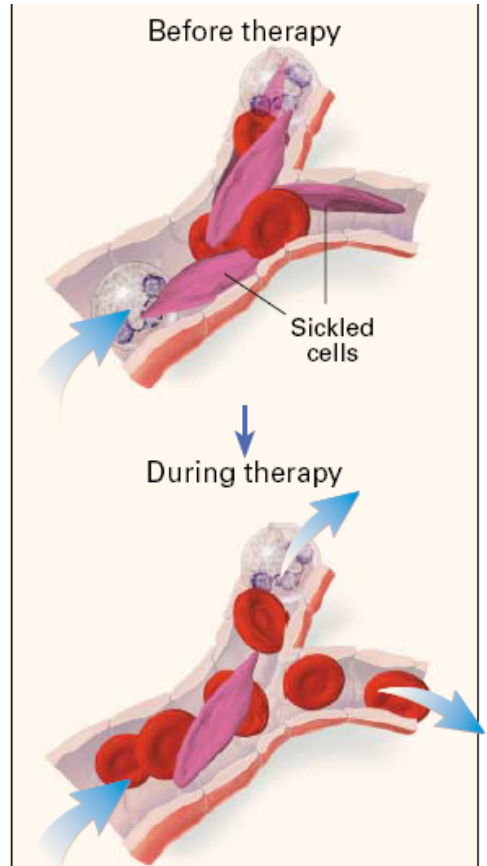
How does hydroxycarbamide work?

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.

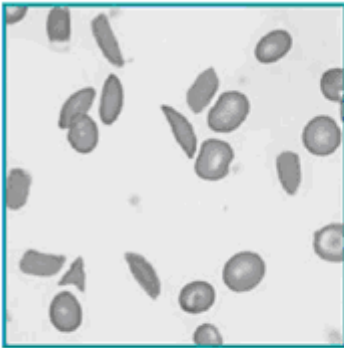
All babies are born with a special type of haemoglobin in their red blood cells called fetal haemoglobin (HbF). Haemoglobin carries oxygen around the body.

- At three months old babies without sickle cell start to make normal adult haemoglobin whereas babies with sickle cell will start to produce sickle haemoglobin.
- Red cells which contain high levels of sickle haemoglobin will turn into sickle red cells.

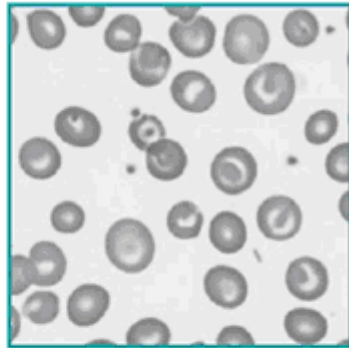


- Fetal haemoglobin helps red blood cells stay round and flexible, allowing them to travel more freely in the blood stream and reducing the clumping / blockages that result in sickle cell crises.
- A high fetal haemoglobin protects the red blood cells from turning into sickle cells.

Hydroxycarbamide raises the amount of fetal haemoglobin in red blood cells, thereby reducing sickling.



Blood cells before taking
hydroxyurea



Blood cells after taking
hydroxyurea

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).

What are the benefits?

Hydroxycarbamide is not a cure for sickle cell disease but can help prevent many of the complications of the disease. It helps to reduce the following:

- number and severity of pain crises
- number of hospital admissions
- number of acute chest syndrome events (chest crisis).
- need for blood transfusions.

It can also:

- increase life expectancy
- improve quality of life.

When will I notice any improvement?

It usually takes at least three months before sickle cell patients can tell if the hydroxycarbamide is working. Hydroxycarbamide **will not** work if you only take it every now and again or only when you are ill or in pain.

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 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.

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 more healthy in myself. I can breathe better, move better and my joints feel better”. NA, male age 28

“Hydroxyurea 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 really excruciatingly painful, but now they’re a lot more manageable. So it really has been life changing, it’s made a massive difference”
ML, male age 45. Using hydroxyurea 8 years.

Side effects and risks

What are the side effects of hydroxycarbamide?

You may experience side effects while taking hydroxycarbamide. Please let your doctor or nurse know if you experience any side effects. Any side effects will be closely monitored by your haematologist or nurse specialist.

Common side effects affect between 1 and 10 out of every 100 people (1-10%)

- anaemia (a fall in the haemoglobin level - this may lead you to become breathless and tire easily).
- a low white cell count (this may increase the likelihood of infection if they are very low) or
- a low platelet count (this may increase the likelihood of bleeding and bruising if they are very low).

The risks of having abnormal blood counts are low, as long as you attend your blood tests. For more information about blood tests during treatment, please see page 12.

Less common side effects affect between 1 and 10 out of every 1 000 people (0.1-1%)

- nausea and vomiting, loss of appetite
- sore mouth, mouth ulcers
- itching and skin inflammation / rash

Rare side effects affect between 1 and 10 out of every 10 000 people (0.01-0.1%)

- gout (pain and inflammation in the joints), most commonly in the toes
- hypersensitive or allergic reactions
- hair loss / thinning

Very rare side effects affect less than one person in 10 000 (less than 0.01%)

- skin discolouration
- wasting of skin and nails

Is there a risk of developing cancer by taking hydroxycarbamide?

Hydroxycarbamide is a mild form of chemotherapy. When used by patients with an abnormal bone marrow who already have an increased risk of developing cancer hydroxycarbamide has been associated with higher rates of cancer.

This effect has **not** been seen in patients with sickle cell. Hydroxycarbamide has been used to treat patients with sickle cell disease since 1995, in many thousands of patients across the world. The rates of cancer in these treated patients is no more than we see in the normal population.

For example, a research study in 2010 by Steinberg found no increased rates of cancer in patients who were treated with hydroxycarbamide for over 17 years.

What is hydroxycarbamide NOT used to treat?

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

- leg ulcers
- bone damage (avascular necrosis)
- infections.

Taking hydroxycarbamide

You will be prescribed the hydroxycarbamide in the clinic by your haematologist or clinical nurse specialist.

Your GP will only prescribe it if they have a special arrangement with the clinic. This would be if you live a long way from the clinic or find it difficult to get to the clinic and your GP is willing to prescribe hydroxycarbamide and monitor your treatment.

How much hydroxycarbamide will I have to take?

Treatment starts at a low dose and is slowly built up if your body tolerates it well. Each capsule contains 500mg hydroxycarbamide.

- Typical doses for adult sickle cell patients range from one to four capsules each day.
- The dose is altered depending on your blood counts and your doctors aim to reach the highest possible dose that your bone marrow will tolerate.
- **If you take more than the amount prescribed this may stop your bone marrow working normally which can cause serious health problems.**

Hydroxycarbamide can be taken with food or on an empty stomach.

Do I have to take hydroxycarbamide all the time?

For hydroxycarbamide to work properly you have to take it every day as directed by your haematologist.

What if I forget to take a dose of hydroxycarbamide?

- Take your normal dose the next day, but **do not take a double dose.**
- Tell your haematologist the next time you go to clinic how many times you have missed a dose.

- If you are sick (vomit) just after taking your capsules, do not take an additional capsule and take your normal dose the next day.

What if I become unwell or have any concerns?

- During office hours you can contact the Sickle Cell Team at Guy's and St Thomas' Hospital on the numbers at the end of this leaflet.
- At other times you will need to contact your GP or attend your Emergency (A&E) Department.

Normally your haematologist will recommend that you restart hydroxycarbamide when your blood count has been checked and is normal.

You should seek urgent medical attention if you have any of the following:

- severe pain or pain that is not responding to your usual painkillers
- pain which different to your usual sickle pain
- a high fever
- shortness of breath, especially if this is associated with chest pain
- other symptoms which you are concerned about.

How long should I take hydroxycarbamide for?

You should continue to take hydroxycarbamide as advised unless your haematologist or another doctor tells you not to. If you want to stop taking it please talk to your haematologist first.

If after a trial period of several months of taking the correct dose there has been no medical benefit to your sickle cell disease your doctors will usually advise you to stop taking the drug.

How will my health be monitored?

As the medication affects red cells, white cells and platelets in the blood you will need regular blood tests and monitoring while you take this medication (blood counts, HbF level, liver and kidney function).

- After starting hydroxycarbamide or after a dose change, you will be seen two weeks later for a blood count check.
- As soon as your blood measures are stable on the hydroxycarbamide you will be seen every eight to twelve weeks.
- Your dose may be reduced if your blood count falls.

We will not be able to prescribe hydroxycarbamide if you are not able to come for regular blood tests as we need to be able to monitor you. The sickle cell team will monitor the blood tests and ask you to decrease or stop the medication if your blood tests become abnormal.

The risks of having abnormal blood counts are low, as long as you attend for regular blood monitoring. If you do not have regular blood monitoring then any abnormalities in your blood count will not be recognised early and this may be dangerous.

Looking after your hydroxycarbamide

- Keep the capsules in a closed container at room temperature away from heat, moisture and direct light.
- Keep the capsules out of the reach of children. They can be harmful if children swallow them.
- Never share your medicine with anyone.
- If you stop taking hydroxycarbamide for any reason, please return your capsules to the pharmacy. Do not throw them in the bin or flush them down the toilet.

Can I take other medications while I am taking hydroxycarbamide?

- You should tell your doctor about all the other prescription or non-prescription medications, vitamins, or herbal preparations you are taking or are planning to take when you start using hydroxycarbamide. Occasionally the dosage will need to be changed because of your other medications.
- You should also tell your doctor if you start any new medications. This includes medicines bought at a pharmacy or elsewhere.

Fertility

Is there any risk to my fertility or pregnancy whilst taking hydroxycarbamide?

For men:

- Hydroxycarbamide does not stop men from having normal erections. It does not prevent you from making a woman pregnant or fathering children.
- A man's sperm count may be reduced and there is a possibility of abnormal sperm being produced while taking hydroxycarbamide. This will usually return to normal after the hydroxycarbamide has been stopped for two to three months.

We recommend that you continue to use contraception while using hydroxycarbamide because the medication can potentially be harmful to the developing fetus.

In one or two cases the sperm count has not returned to normal, even when hydroxycarbamide was stopped for over a year. We therefore recommend that you have a sperm sample checked and stored before you start hydroxycarbamide. Your haematologist can arrange this.

For women:

- Women should not become pregnant while they or their partner is taking hydroxycarbamide as research suggests that there is a possibility of fetal abnormalities. You should use an effective form of contraception to avoid pregnancy.
- You can ask your GP, practice nurse or the sickle cell team for further advice.
- If you become pregnant you must stop the hydroxycarbamide and tell your haematologist.

What if my partner and I want to have a baby?

If you or your partner is taking hydroxycarbamide, you should stop taking it at least three months before trying to conceive. This will reduce the risk to your baby. **You must discuss this with your haematologist.**

Can I breastfeed my baby while taking hydroxycarbamide?

You **should not** breastfeed while taking hydroxycarbamide as small amounts of the drug may be present in your breast milk. You can either breastfeed and not take hydroxycarbamide or bottle feed your baby and start taking hydroxycarbamide again.

You should discuss this with your haematologist before making a decision.

Important information

Please note that this leaflet does not describe sickle cell disease in detail. If you need more information on sickle cell disease, please contact the South East London Sickle Cell & Thalassaemia Centre on 020 7414 1363. An information leaflet is provided by the manufacturer in each box of medicine. It is important that you read both the manufacturer's leaflet and this information sheet.

The brand of hydroxycarbamide that we prescribe at Guy's and St Thomas' NHS Foundation Trust is not licensed for the treatment of sickle cell disease. Your consultant will discuss this with you in more detail. For further information on unlicensed medicines, please ask for a copy of our trust leaflet **Unlicensed medicines – a guide for patients**, or contact our Pharmacy Helpline (contact details at the end of the leaflet). If you have any questions or concerns, please do not hesitate to speak with the haematologists (blood specialists), sickle cell specialist nurses, day unit nurses or health psychologists.

Sickle cell team contacts

The telephone numbers below are available Monday-Friday, 9am-5pm. Outside these hours, please contact your GP or go to your local Emergency Department (A&E).

- **Haematology Clinic** t: 020 7188 2743 / 2724
- **Haematology Day Unit** t: 020 7188 2745 / 2710
- **Consultant Haematologists** t: 020 7188 2741
- **Specialist Registrar** t: 020 7188 7188 **bleep** 0248
- **Senior House Officer (SHO)** t: 020 7188 7188 **bleep** 2283
- **Advanced Nurse Practitioner** t: 020 7188 2710 **bleep**1843 **mob** 07770 683947
- **Advanced Nurse Practitioner (Adolescent)** t: 020 7188 2710 **bleep** 2256 **mob** 07770 678851
- **Clinical Nurse Specialist** t: 020 7188 2710 **bleep** 2868 **mob** 07920 711266

- **Psychologists**

Clinical Health Psychologist **t:** 020 7188 2718

Health Psychologist **t:** 020 7188 2718

- **Sickle Cell Support Group:** every Tuesday evening, 6 – 7.30pm, Haematology Seminar Room

For more information leaflets on conditions, procedures, treatments and services offered at our hospitals, please visit www.guysandstthomas.nhs.uk/leaflets

Pharmacy Medicines Helpline

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

t: 020 7188 8748 9am to 5pm, Monday to Friday

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.

t: 020 7188 8801 (PALS)

e: pals@gstt.nhs.uk

t: 020 7188 3514 (complaints)

e: 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 get in touch:

t: 020 7188 8815

e: languagesupport@gstt.nhs.uk

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

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