

Hydroxycarbamide (Hydroxyurea, HU) in sickle cell disease (SCD)

Patient education tool



What is HU?

A disease modifying medication taken long-term as once daily capsule(s) by mouth to reduce the severity of sickle cell disease by gradually improving symptoms and blood results over several months. If treatment is stopped, the beneficial effects wear off within 2 months.

Who should be offered HU?

BSH Guideline, May 2018

- HbSS and HbSβ⁰ infants from 9 months - **offer regardless of clinical severity**
- HbSS and HbSβ⁰ children and adults - **consider regardless of clinical severity**
- >3 pain episodes in a year, interfering with daily activities and quality of life (QOL)
- After an episode of acute chest syndrome – to help prevent further episodes
- After a transfusion program for previous abnormal Trans Cranial Doppler
- Sickle kidney disease with protein in the urine
- Those with low oxygen saturations – which often improve with HU treatment
- Anaemia – HU treatment usually leads to improved haemoglobin levels

Why?

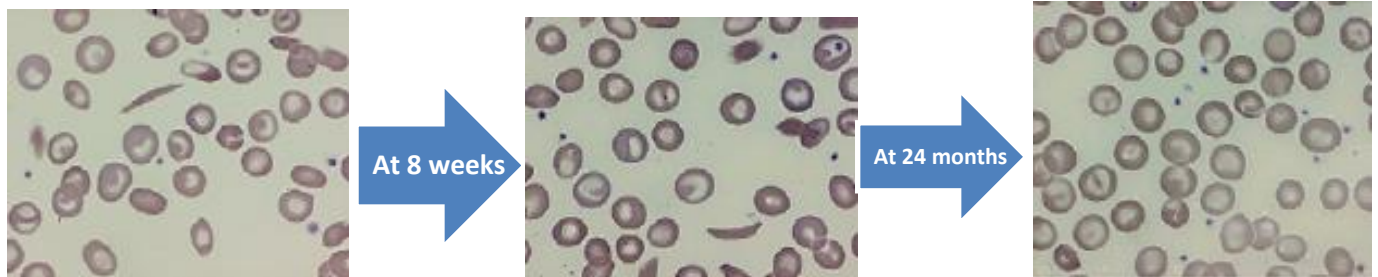
- **Longer life expectancy**
- Fewer and less severe pain episodes
- Less organ damage and jaundice
- Fewer hospital admissions, transfusions, acute chest crises
- Improved weight, wellbeing, higher haemoglobin, improved exercise tolerance

How?

HU makes red blood cells bigger and more flexible and less likely sickle by increasing hemoglobin F and reducing haemoglobin S. Monitoring includes blood tests (full blood count, retics, kidney and liver function) 2 weeks after starting or significant dose changes, and then about every 12 weeks

Blood changes on hydroxycarbamide:

- Reduced numbers of sickle cells
- Higher haemoglobin
- Larger red blood cells (higher mean cell volume – MCV)
- Higher foetal haemoglobin, HbF (and lower sickle haemoglobin)



Before HU

Low Hb of 76 g/l
MCV 84 Fl
HbF 6%
Frequent sickled cells

After 8 weeks

Improving Hb of 82 g/l
Large red cells, MCV 96 Fl
HbF 8%
Occasional sickle cells

After 24 months

Near-normal Hb of 114 g/l
Large red cells, MCV 113 Fl
HbF 24%
No sickled cells

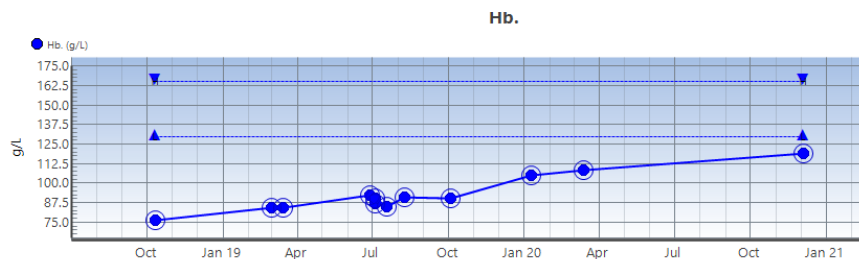
Safety: After more than 30 years of clinical experience and trials there have been no significant long-term toxicities in SCD, and no increase in cancer or leukaemia

Fertility

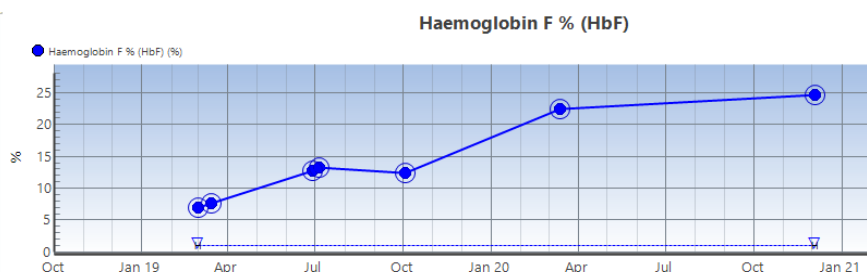
- Contraception is advised during treatment and most plan to stop HU treatment 3 months before conception and consider alternative treatments, such as transfusion
- Normal births have occurred despite HU treatment during pregnancy or at conception
- Female fertility is not usually affected; some males have reduced sperm so are offered sperm banking (automatic NHS eligibility if <40 years) but HU does not affect sexual function such as erections, orgasms or desire.

Improving results during treatment with hydroxycarbamide:

- Haemoglobin gradually improves on treatment:



- Increased HbF% gradually improves with treatment; higher HbF prevents sickling



Before HU

After HU

Yellow jaundice of eyes often clears on HU treatment



Side effects:

- Well tolerated with no serious long-term toxicity
- Occasional nausea and bowel upset, avoided by taking HU at night after food
- Headache on starting medication, which improves with time +/- dose reduction
- Rarely thinning of hair, which reverses when the medicine is stopped
- Reversible reduction in blood cells, which is why regular blood tests are needed
- Darkening of nails and skin, which depends on dose and reverses after stopping, dry skin

Temporary darkening of nails can occur with HU



A dosette box can help you take medication every day

Published studies of benefits of hydroxycarbamide in SCD: 9 yr follow up (MSH study JAMA 2003; 289:1645.), 40% reduction in mortality; 17.5 yr follow up (Am J Hematol 2010; 85:403), mortality 43% with, 87% without HU; BABY HUG trial (Lancet 2011; 377:1663.) from 9 months of age