## 1. Introduction and Who Guideline applies to

This guideline has been developed to advise clinicians and multi-discilpinary team members involved in the care of patients with sickle cell disease. It has been developed alongside the East Midlands Sickle Cell and Thalassaemia network guidelines, taking more recent national guidance into account. It outlines the management of hydroxycarbamide therapy in patients with sickle cell disease, with particular focus on the following:

- Indications for treatment
- Exclusions to treatment
- Prescribing process
- Monitoring including SOP for nurse led clinic
- Side effects

## 2. Guideline Standards and Procedures

### *Indications for treatment:*

Hydroxycarbamide is a disease modifying therapy for patients with sickle cell disease. In line with national guidance it should be offered to the following:

1) All adults with HbSS/SB0 thalassaemia with recurrent acute crises (>3 admissions in 1 year or very symptomatic in the community)
2) All adults with HbSS/SB0 thalassaemia and a history of severe and/or recurrent acute chest syndrome
3) Consider in other genotypes (non-SS/SB0) for the above indications listed in 1) and 2)
4) Consider in adults with sickle cell disease (all genotypes) with other indications in line with current national standards after discussion at regional MDT. This may include (not an exclusive list):
    a. Patients with sickle nephropathy with persisting proteinuria despite ACEi/ARB therapy
    b. Patients with chronic, symptomatic anaemia which interferes with daily activities or affects quality of life

It may also be started in childhood routinely or if a child has had previously abnormal TCD velocities and completed at least 1 year of transfusion treatment in the absence of abnormal cerebral vasculopathy on MRI (TWiTCH protocol). When these children transition to adult services, hydroxycarbamide should be continued following the same follow up criteria as below.

### *Exclusions:*

1) Pregnancy
2) Active hepatitis
3) Unable to use adequate contraception
4) Unable to take regular medication/ attend for monitoring

***Process for initiation and prescribing:***

1) Provide written information (Patient leaflet available- appendix 1)
2) Males only: offer sperm analysis and storage prior to initiation (Refer to ACU – appendix 2)
3) Baseline FBC, reticulocyte count, HbF%, U&E, LFT, LDH
4) Refer to monthly haemoglobinopathy MDT to discuss treatment initiation
5) Document informed consent
6) Baseline pregnancy test in post-pubertal women
7) Start at dose of 15mg/kg /day (to nearest 500mg)
8) Refer to nurse led clinic to review FBC and reticulocyte count at 2 weeks
9) Medical clinic appointment at 6 weeks
10) Ongoing follow up in line with BSH guideline (see appendix 3 for nurse led clinic SOP)

Cautions:

1) If Hb >3g/dl above baseline stop hydroxycarbamide and consider venesection
2) Increase monitoring frequency if there is a downward trend in FBC parameters
3) Use with caution in renal impairment, commence at 50% dose if CrCl <60ml/min
4) Ask patients regarding contraception use at every visit
    a. If pregnancy occurs in a female patient, stop hydroxycarbamide and monitor pregnancy. Consider switching to a transfusion programme for the remainder of the pregnancy. Refer to haematology obstetric clinic for ongoing pregnancy management and refer to clinical MDT for discussion

    b. If a pregnancy is being planned, stop hydroxycarbamide at least 3 months prior to planned conception (both male and female patients, although this should be reviewed if severe spectrum disease)

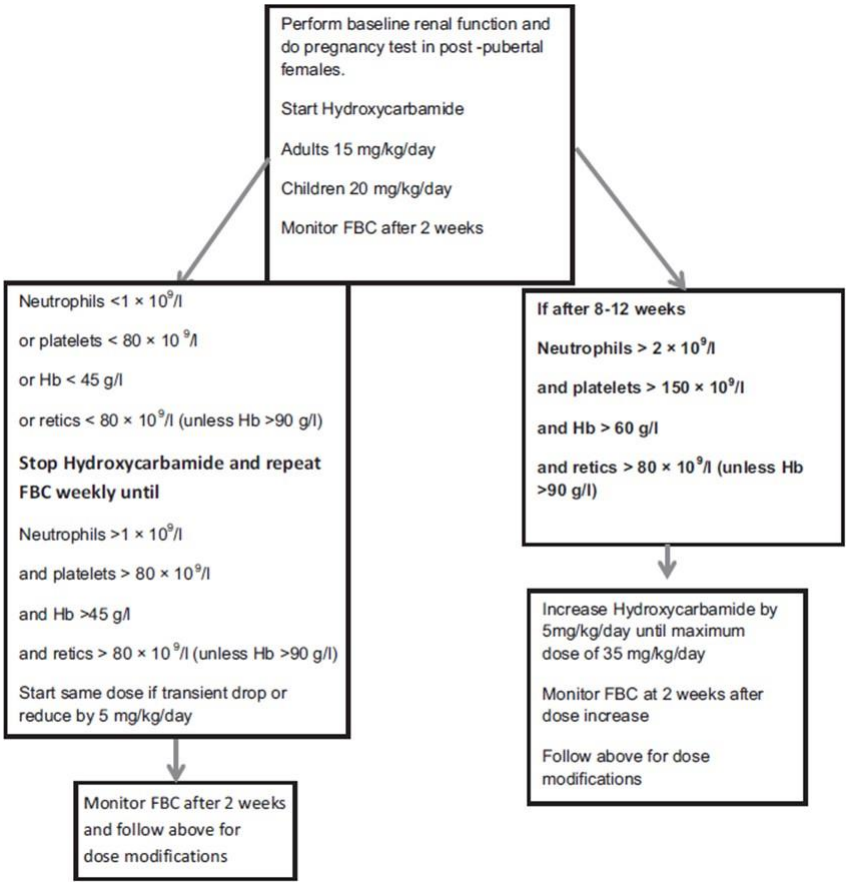
***Monitoring***

Monitor in line with flow chart (taken from BSH 2018 guideline).

At each visit complete the following checklist:

| | |
|---|---|
| Current daily dose (calculate mg/kg) | |
| Side effects review | Yes / No Details: |
| Clinical benefit | Yes / No HbF%: Date: |
| Follow up blood tests<br>Date: | Hb: Neut: Plt:<br>Retics: LFT: eGFR: |
| When was dose last changed? | |
| What is the maximum tolerated dose? | |
| Dose change indicated? | Yes / No Details: |
| Hydroxycarbamide booklet completed?? | Yes / No |
| Follow up arranged | Yes / No Date: |
| Repeat bloods reviewed | Yes / No Date: |

After any dose change, bloods should be repeated after 2 weeks. Dose modifications should occur in line with the following monitoring protocol (Taken from BSH guideline):




The aim of treatment is to maximise HbF% without adverse myelosuppression but if patient has had clinical benefit (even with low HbF%) then hydroxycarbamide should be continued. Incremental dose increases can occur to the maximum tolerated dose in line with above flow chart to the maximum dose of 35 mg/kg.

Hydroxycarbamide for use in sickle cell disease as a shared care agreement has been approved by LMSG. Initial prescribing will be done through UHL, but at the discretion of the consultant haematologist a SCA maybe requested. The ongoing responsibilities of UHL as outlined in the LMSG document which include the need for written communication of dose changes and updating of hand held records (where applicable).

### *Side effects:*

Common: myelosuppression, hyperpigmentation of nails, nausea and vomiting, skin rash, diarrhoea

Uncommon: Alopecia, Teratogenicity, Potential for reduced sperm count and function, Potential low risk of second malignancy, but no evidence of increased leukaemogenesis

## 3. Education and Training

Rolling education programme for haematology trainees in East Midlands South region – to be provided by designated haematology team member

## 4. Monitoring Compliance

| What will be measured to monitor compliance | How will compliance be monitored | Monitoring Lead | Frequency | Reporting arrangements |
|---|---|---|---|---|
| Audit of hydroxycarbamide use in sickle cell disease | Registered audit with clear quality improvement outcome measures | Amy Webster/Jessica Gunn | 2 yearly | Via trust audit protocol |

## 5. Supporting References

EMSTN Hydroxycarbamide in sickle cell disease guideline

British Society of Haematology: Guidelines for the use of hydroxycarbamide for children and adults with sickle cell disease *British Journal of Haematology* 2018;181(4):460-475

LMSG shared care agreement:

https://www.lmsg.nhs.uk/wp-content/uploads/2015/05/Hydroxycarbamide_SCA.pdf

## 6. Key Words

Sickle cell disease, hydroxycarbamide

| CONTACT AND REVIEW DETAILS | |
|---|---|
| **Guideline Lead (Name and Title)**<br><br>Amy Webster, Consultant Haematologist | **Executive Lead**<br><br>CHUGGS Q&S Board |
| **Details of Changes made during review:**<br><br>Updated patient information leaflet information<br>Updated information relating to nurse led clinic frequency | |

## Appendix 1: Patient information leaflet

Up to date patient information leaflet can be downloaded from Your Health at:

Hydroxycarbamide treatment plan for haemoglobin disorders (leicestershospitals.nhs.uk)

## Appendix 2: ACU referral

Tel: 0116 2585922
Fax: 0116 2587688
E-mail : enquiries@leicesterfertilitycentre.org.uk
Web : www.leicesterfertilitycentre.org.uk

**HFEA Centre Number 0068**

Please ensure patient has been swabbed for COVID-19 antigen testing prior to referral.

**Referral Form for Oncology Patients – Sperm, Egg or Embryo Storage**

Date:.....

Unit number:..... NHS number: .....

Name:..... Date of birth:.....

Address:.....

.....

.....

Patient telephone number:.....

Reason for referral:.....

.....

Proposed treatment:.....

Treatment start date:.....

If breast cancer, hormone receptor status:.....

Has patient had any previous chemo- or radiotherapy? .....

If so what & when:.....

Referring doctor/nurse:.....

Referring department:.....

Referring hospital:.....

Name of Consultant:.....

Department telephone number:.....

**PLEASE FAX THIS FORM TO ASSISTED CONCEPTION UNIT (FAX: 0116 258 7688)**

☐ **Department aware of referral costs** (Please tick the relevant boxes)

☐ **HIV, HTLV-1, Hep B (Core antibody & Surface antigen), Hep C & Syphilis test**

☐ **Advised male patients to leave 2-3 days sexual abstinence if possible**

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02/06/2020

## Appendix 3 – SOP for Haemoglobinopnurse led clinic (v1 October 2020)

*Purpose:*

- Telephone clinic for the remote monitoring of patients on hydroxycarbamide and/or follow up for those patients following hospital discharge.
- Weekly clinic held on Friday morning at Leicester Royal Infirmary.
- Maximum of 4 patients per clinic list

*Inclusion Criteria:* The following **must** be met for patients to be eligible for nurse led follow up:

- Aged 18 years or older.
- Referred to the nurse-led monitoring clinic from a Consultant or SpR haematologist by entry in medical notes, electronic patient records or via clinic letter.
- Have a valid prescription of hydroxycarbamide on Chemocare or valid shared care agreement with GP
- Presence of valid consent form and documented explanation from the relevant medical staff of the purpose of treatment, the monitoring procedure required and potential adverse side effects.
- Have had a detailed medical history taken and medical examination where necessary performed by the medical staff
- Have a full list of current medications documented in medical notes or electronic patient records
- Have been informed by medical staff of all necessary precautions when taking the prescribed treatment.
- Have all preliminary investigations relevant to treatment carried out and documented in the medical notes or electronic patient records
- Have clear documentation of the planned drug dosage regimen and proposed follow up schedule in the medical notes or electronic patient records.
- Patients must be on stable doses and compliant with their medication.
- Patients who are post inpatient and need a follow up phone call, with clear guidance on discharge letter regarding specific concerns that may require follow up input

*Exclusion Criteria:*

- Concerns regarding patients with complex needs, issues around compliance and new patients starting treatment.
- Patients who decline nurse led follow up or do not engage with service. These patients will be referred back to the medical clinic for ongoing management.

*Process for nurse led clinic:*

1. Patient referral made via the following routes only:
    a. Consultant Medical clinic (AHWHD or AHWAR)
    b. Following hospital discharge (MUST be discussed and agreed with CNS and/or Dr Webster/Dr Wharin)
2. Patient booked into available clinic slot. No overbooking permitted.
3. Telephone clinic completed as per clinic template:
    a. Clinical management of hydroxycarbamide in line with UHL guideline
    b. Any concerns regarding hydroxycarbamide dosing (either escalation or reduction) must be discussed with a senior haematologist (Consultant or SpR).
    c. Abnormal blood results (outside of those anticipated due to treatment) should be discussed with a senior haematologist prior to discussion with patient
    d. If clinical concerns, to escalate to Dr Webster/Dr Wharin or Haematology attending consultant (if Haemoglobinopathy team unavailable).
    e. Outcome of clinic discussion to be communicated via clinic letter, outlining written advice to GP regarding dosing.

4. Follow up:
    a. All patients on hydroxycarbamide will require a minimum of 4 clinic visits per year. 2 clinic appointments will be nurse led and 2 clinics will be Consultant led (1 of which will be an annual clinic appointment).
    b. If additional visits are required (due to dose changes or abnormal blood results) this will be clearly documented in the medical clinic.
    c. If a patient cannot be contacted by telephone, a follow up appointment in the nurse led clinic can be made providing there are no clinical concerns. After a second DNA appointment, patients must be rebooked into the medical follow up clinic.
    d. If a patient is booked for clinic but has not had the necessary blood tests, this will be highlighted to the medical team and GP. Any patient who has not had blood tests in the preceding 4 months will be escalated to the consultant haematologist, who will highlight to GP (if shared care agreement in place) or to patient directly (if prescribed by UHL).