# Blood transfusion and management of iron overload in patients with Sickle Cell Disease and Thalassaemia

| **Profile** | |
|---|---|
| **Version:** | *V3.0* |
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| **Executive/Divisional sponsor:** | *Dr Lisa Pickering, Divisional Chair* |
| **Applies to:** | *All staff involved in the care of patients with Sickle Cell Disease* |
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| **Approval** | |
| **Approval person/Committee:** | *MedCard Divisional Governance Board* |
| **Date:** | *14th February 2019* |

# Contents

## Policy Gateway

Please complete the checklist and tables below to provide assurance around the policy review process.

☒ I have involved everyone who should be consulted about this policy/guidance

☒ I have identified the target audience for this policy/guidance

☒ I have completed the correct template fully and properly

☒ I have identified the correct approval route for this policy/guidance

☒ I have saved a word version of this policy/guidance for future reviews and reference

| Please set out what makes you an appropriate person to conduct this review: |
| --- |
| Consultant for Adult Haemoglobinopathy service |

Please set out the legislation, guidance and best practice you consulted for this review:

- West Midlands Review Service – Quality Standards: Health Services for People with Haemoglobin Disorders (2018/19)
- Standards for the Clinical Care of Adults with Sickle Cell Disease in the UK 2018 (Sickle Cell Society) https://www.sicklecellsociety.org/wp-content/uploads/2018/04/Web-version-FINAL-SCS-Standards-GSM-6.4.18.pdf
- British Society Haematology : guidelines Red Cell Transfusion in Sickle Cell Disease Part I and Part II (7.11.17 and 18.11.18) https://b-s-h.org.uk/guidelines/guidelines/red-cell-transfusion-in-sickle-cell-disease-part-I/

| Please identify the key people you involved in reviewing this policy why, and when: |
| --- |
| |

| Summarise the key changes you have made and why: |
| --- |
| Updates in line with the UK standards of care for SCD<br>Updated contact details |

## Executive Summary

Transfusion in patients with Sickle Cell Disease (SCD) and thalassaemia is increasing rapidly across the UK but with variability in indications and lack of robust evidence in many cases. Guidance is now issued by both the British Standards of Haematology (2016) and from the Standards of Clinical Care for adult patients with SCD in the UK. These guidelines describe the indications, management and process (including safety and selection) for blood transfusion in SCD and thalassaemia. The guideline also covers managements of the consequences of transfusion – predominantly iron overload and the need for iron chelation.

## 1. Introduction

Transfusion in patients with Sickle Cell Disease (SCD) and thalassaemia is increasing rapidly across the UK but with variability in indications and lack of robust evidence in many cases. Guidance is now issued by both the British Standards of Haematology (2016) and from the Standards of Clinical Care for adult patients with SCD in the UK. These guidelines describe the indications, management and process (including safety and selection) for blood transfusion in SCD and thalassaemia. The guideline also covers managements of the consequences of transfusion – predominantly iron overload and the need for iron chelation.

These guidelines should be used in conjunction with the St George's University Hospitals NHS Blood Transfusion Policy http://stg1wordpress01/wordpress/wp-content/uploads/2016/06/Blood-Transfusion-Adults.pdf

## 2. Status and Purpose

This document is part of the Haematology Department's guidelines on the management of patients with SCD and is applicable to all staff involved in the care of these patients.

## 3. Definitions

Sickle Cell Disease – inherited lifelong condition due to abnormal haemoglobin variant.

## 4. Scope

This guideline is relevant to the care of patients with SCD requiring elective and emergency surgery at St.George's.

## 5. Roles and Responsibilities

**5.1 Haemoglobinopathy team (Consultant haematologists, Clinical Nurse Specialist and Clinical Health Psychologist)** – Responsible for the care of these patients, developing and updating guidelines to be reflective of good practice and to deliver the training to ensure good safe care.

**5.2 Medical staff involved in the care of patients with SCD.** Responsible with the oversight of the haemoglobinopathy team to deliver the care to these patients in line with guidelines where possible.

**5.3 Nursing staff and allied health professionals involved in the care of patients with SCD on wards, day unit and other areas of St George's** responsible with the oversight of the haemoglobinopathy team to deliver the care of these patients in line with guidelines where possible.

## 6.0 Content

- In patients with **sickle cell disease** (SCD) the transfusion of packed red cells has 2 goals:
  1) To increase tissue oxygenation by correcting anaemia
  2) To prevent or reduce the complications of sickling by reducing the HbS% content of the blood

"Top up" transfusions are generally required to achieve the first aim. Exchange blood transfusions usually achieve the second goal.

- Patients with **β thalassaemia major (transfusion dependent thalassaemia, TDT)** do not produce sufficient haemoglobin to sustain healthy growth and so require regular red cell transfusions, usually with a regimen of around 2-4 units every 2-4 weeks. The goal in these patients is to maintain a pre-transfusion Hb of greater than 95g/L to maintain good health, reduce bone marrow expansion and to minimise the development of iron overload.

- Patients with **β thalassaemia intermedia (non transfusion dependent thalassaemia, NTDT) or HbH disease (α thalassaemia)** may need intermittent transfusions at times of physiological stress or need (eg pregnancy, puberty) – these patients' requirements will be decided on individual clinical grounds.

All **unplanned transfusions** for patients with sickle cell disease or thalassaemia must be discussed with the haematology team caring for the patient. In patients with sickle cell disease, mild anaemia does not usually require correction by blood transfusion

The **blood transfusion laboratory** must be made aware that the recipient patient has sickle cell disease or thalassaemia so that extended phenotyping can be done and appropriately crossmatched and sickle negative blood can be provided. These patients are not suitable for rapid cross match.

All patients with a haemoglobinopathy should, at their first engagement with the hospital, have a sample sent to the blood transfusion laboratory for a full, extended red cell antigen phenotype (and genotype where possible) as well as the standard ABO and Rh blood group.

**Guidelines on red cell transfusion in sickle cell disease. Part I: principles and laboratory aspects (BSH) – Summary of Key Recommendations (November 2016)**

- The decision to top up or exchange transfuse an adult or paediatric patient with sickle cell disease (SCD) needs the input of a clinician with appropriate experience. Specialist advice should be obtained for the management of patients with complex transfusion requirements

- Transfusion in SCD requires careful consideration of both the haemoglobin concentration (Hb) and/or percentage of sickle haemoglobin (%HbS) in order to ensure maximal oxygen

delivery to tissues without increasing overall blood viscosity to detrimental levels

- A transfusion history should be obtained in all SCD patients requiring transfusion, whether elective or emergency. Close communication is essential between clinical and laboratory teams so that appropriate blood is given

- Individuals with SCD are high-risk surgical patients. Close liaison between all clinical teams is essential with preoperative optimisation and appropriate postoperative care, whether transfused or not

- Virology testing [hepatitis B, hepatitis C and human immunodeficiency virus (HIV)] should be undertaken at presentation and hepatitis B vaccination should be given to all patients with SCD, irrespective of previous or prospective planned transfusions. SCD patients on regular transfusions should be screened annually for hepatitis B, hepatitis C and HIV

- The choice of transfusion method, i.e., simple (top up) or exchange, should be based on clinical judgement of individual cases, taking into account the indication for transfusion, the need to avoid hyperviscosity and minimise alloimmunisation, maintenance of iron balance, venous access issues and available resources

- All hospitals that are likely to admit SCD patients should have staff trained in manual exchange procedures and clearly identified manual exchange procedures, as this can be lifesaving in emergency situations

- Large referral centres managing patients with SCD should have facilities and trained staff for automated exchange transfusion

- If transfusion is needed, patients with SCD should be given ABO-compatible, extended Rh- and Kell-matched units. If there are clinically significant red cell antibodies (current or historical) then the red cells selected should be negative for the corresponding antigens

- Patients with SCD must also have extended red blood cell (RBC) antigen typing performed, which may assist with further serological testing and selection of red cell units if there are haemolytic reactions and complex transfusion requirements

- Blood provided for SCD patients should be HbS negative and, where possible, should be <10 days old for simple transfusion and <7 days old for exchange transfusion but older blood may be given if the presence of red cell antibodies makes the provision of blood difficult

- All patients with SCD should carry a transfusion card indicating that they have ‘special requirement’ and, in particular, giving information of any alloantibody.

- Patients with multiple red cell alloantibodies or antibodies to rare antigens need a clear agreed plan given that blood may be difficult to source in the elective or emergency setting. Close liaison between all clinical teams, the hospital transfusion laboratory and the national blood service is essential to ensure appropriate provision of blood.

- All clinicians managing patients with SCD should be aware of the risk of haemolytic transfusion reactions to ensure prompt recognition and management. Close liaison is needed with haemoglobinopathy specialists and blood services for investigation and management.

- Any adverse events or reactions related to transfusion should be appropriately investigated and reported to local risk management systems and to UK Haemovigilance Schemes

# INDICATIONS FOR TOP UP TRANSFUSIONS

## SICKLE CELL DISEASE

- Symptomatic anaemia (eg haemolysis, sequestration, acute parvovirus infection)
- Consider if Hb <60g/L or if fall from baseline is greater than 20g/L
- Before surgery in some cases in discussion with the sickle cell team and as per their preoperative surgical plan

## β THALASSAEMIA

- As part of regular transfusion programme or if Hb has fallen less than 95 g/L in TDT
- At specific times for those with NTDT when a higher Hb is required

In patients with SCD who have an Hb >90g/L, top up transfusions should be avoided in patients to avoid the risk of hyperviscosity. The target post-transfusion Hb should usually be around 90-100g/L or the patient's own baseline Hb.

Patients with TDT receiving regular transfusions are managed on the ruth myles day unit. Monitoring should include review of pre transfusion Hb levels with an aim for the pre transfusion Hb to be >95g/L as well as ferritin levels

Venous access is usually peripheral with the aid of ultrasound guidance and should be achieved within 3 attempts (though if more than once is required regularly this should be escalated). Wherever possible ports and indwelling central lines should be avoided in patients with TDT due to increased risk of line thrombosis and infection

**INDICATIONS FOR ELECTIVE EXCHANGE TRANSFUSIONS IN SCD**

- Secondary stroke prevention
- Primary stroke prevention (ongoing transfusion programme from childhood)
- Before elective surgery after discussion with the haematology team

*Consider also in*

- Pregnancy
- Recurrent pain or chest crises not responding to hydroxycarbamide
- Pulmonary hypertension
- Refractory leg ulcers
- Refractory sickle nephropathy / post renal transplant
- Persistent priapisms

All patients being considered for elective exchange transfusions should be discussed at MDT

# INDICATIONS FOR EMERGENCY EXCHANGE TRANSFUSIONS IN SCD

If Hb <60g/L then a top-up transfusion may be considered initially

In most cases, the target Hct is 30-33% and HbS% < 30%

- Acute stroke
- Acute chest syndrome
- Severe sepsis and acute multi-organ failure
- Progressive intrahepatic cholestasis/Right upper quadrant syndrome
- Hepatic sequestration
- Fulminant priapism not responding to urological intervention

At SGH emergency exchange transfusions are usually automated. The decision to perform an exchange transfusion should be made by the haematology registrar in liaison with the haematology consultant for haemoglobinopathies or the on call haematology team out of hours.

The haematology SpR will contact the on call apheresis team, organise venous access and liaise with the blood transfusion laboratory.

Any patient requiring emergency exchange transfusion will need to be on an HDU bed as a minimum so discussion with critical care is essential. This must happen before agreeing to transfer a patient from another site.

The post transfusion target Hct should be no higher than 33% and HbS% should be <30%.

If it is not possible to perform an automated exchange, then a manual exchange can be done and the guidelines for this follow.

See below for link to South Thames Sickle Cell and Thalassaemia Network (STSTN) guidelines on manual exchange guidelines. A copy is also available on the haematology: sickle cell and thalassaemia intranet page

http://www.ststn.co.uk/wp-content/uploads/2012/02/Manualebt-March09Gstt-kch-luh_web-version.pdf

**Guidelines for SCD patients on long term transfusions**

- Blood safety
  - Hepatitis B vaccination and titre checks annually
  - Annual HIV Ag and Ab test
  - ABO-compatible, extended Rh- and Kell-matched units. If there are clinically significant red cell antibodies (current or historical) then the red cells selected should be negative for the corresponding antigens
  - Less than 10 days old if possible.

- Patient Monitoring

  At SGH there are quarterly documented meetings with apheresis nursing staff and medical staff to discuss patients who are on regular transfusion programmes:
  - Any predicted issues
  - Any reported issues
  - Venous access concerns
  - Acceptable Hct and S% levels in patients with SCD
  - Acceptable pre-transfusion Hb levels in thalassaemia patients
  - Review of chelation
  - Review of clinic attendance
  - Discussion of transfusion and patient associated audits
  - Referral of new patients to an apheresis programme
  - Referral of new patients to a top up transfusion programme
  - Transition of patients from paediatrics to adult care
  - Patients stopping a transfusion programme
  - Any emergency procedures in the preceeding time frame.

SCD Patients on long term transfusions should be having automated red cell exchanges unless contraindicated

Venous access is usually via ultrasound guided peripheral access – if hard to find after 3 attempts then discussion about central access with the patient should occur

# Iron Monitoring and Treatment in Patients with SCD and Thalassaemia

## MONITORING

Nearly all patients with TDT will be receiving chelation by adulthood having started treatment in early childhood. Iron levels need to be monitored in these patients in order to guage the efficiency of their chelation regimen, ensure timely changes are made as needed and to assess compliance.

Other patients with haemoglobinopathies should have regular monitoring of ferritin levels: if the patient is **not** on a regular transfusion programme then this is done as part of the annual review. If the patient **does** receive regular transfusions then ferritins should be measured at each transfusion and reviewed at day unit meetings and with the patient in clinic.

Imaging in patients on a transfusion programme: T2* MRI scans to assess liver and cardiac iron loads at St George's Hospital – can be requested via iClip and are performed by the MRI scanner in neuroradiology, Atkinson Morley Wing.

| | |
|---|---|
| No cardiac or liver iron. Stable or falling ferritin | Scan every 2 years |
| No cardiac or liver iron. Rising ferritin | Scan annually until stable |
| No cardiac iron. Moderate liver iron | Scan annually |
| Cardiac involvement | Scan annually |
| Moderate to severe cardiac iron, poor compliance, rising ferritin | May need scan at 6 months |

Chelation should be considered when more than 20 units of blood have been transfused, the serum ferritin is over 1000 or there is radiological evidence of iron overload.

**Patients with TDT** will have annual cardiac reviews (with echocardiograms and cardiac MRIs) and endocrine reviews (with pituitary screening and glucose tolerance tests)

**Patients with SCD** should be referred for a cardiology opinion if there are concerns regarding cardiorespiratory symptoms, abnormal echocardiograms and abnormal MRI scans demonstrating cardiac iron overload. They should also be referred to the endocrinology team if there are concerns regarding pituitary or hormonal disturbance which may be due to iron overload

# TREATMENT OF TRANSFUSION RELATED IRON OVERLOAD

*All doses and dose adjustments should be confirmed with up to date product literature and the British National Formulary. They should also be discussed with the haematology consultant managing that patient.*

## ***Deferasirox (Exjade)***

Deferasirox is an oral iron chelator licensed in sickle cell and thalassaemia patients with iron overload.

Prescriptions for deferasirox should only be initiated after consultation with haematology consultant. Deferasirox is a hospital only prescription. It is indicated for the treatment of chronic iron overload in patients with BTM who are older than 6yrs and in patients with sickle cell anaemia with chronic iron overload in whom
desferrioxamine is contraindicated or considered inadequate.

*Dose*

| | **Film-coated tablets/granules** | **Transfusions** | **Serum ferritin** |
|---|---|---|---|
| **Starting dose** | **14 mg/kg/day** | After 20 units (about 100 ml/kg) of PRBC | >1,000 µg/l |
| **Alternative starting doses** | 21 mg/kg/day | >14 ml/kg/month of PRBC (approx. >4 units/month for an adult) | |
| | 7 mg/kg/day | <7 ml/kg/month of PRBC (approx. <2 units/month for an adult) | |
| For patients well managed on deferoxamine | One third of deferoxamine dose | | |
| **Monitoring** | | | **Monthly** |
| **Target range** | | | **500-1,000 µg/l** |

*Dose alterations due to response*

| | | | |
|---|---|---|---|
| **Adjustment steps** (every 3-6 months) | **Increase** | | |
| | 3.5 - 7 mg/kg/day<br>Up to 28 mg/kg/day | | >2,500 µg/l |
| | **Decrease** | | |
| | 3.5 - 7 mg/kg/day | | <2,500 µg/l |
| | In patients treated with doses >21 mg/kg/day | | |
| | - When target is reached | | 500-1,000 µg/l |
| **Maximum dose** | **28 mg/kg/day** | | |
| **Consider interruption** | | | **<500 µg/l** |

*Dose alterations due to renal impairment*

- See current SPC

*Dose alterations due to hepatic impairment*

- Interrupt treatment if persistent or progressive increase in liver enzymes.

*Contraindications*

Deferasirox should not be used in combination with other chelators
It is contraindicated in patients with a creatinine clearance <60ml/min

*Monitoring / Tests*

- Prior to initiating treatment, the patient requires serum ferritin, renal and liver biochemistry. Audiology and ophthalmology review
- In first month, renal and liver biochemistry every 2 weeks
- Every 4-8 weeks, ferritin, renal and liver biochemistry
- Urine dip for protein assessment

***Desferrioxamine (Desferal)***

Desferrioxamine is the first line chelator in patients with sickle cell anaemia and chronic iron overload secondary to repeated blood transfusions.

*Dose*
• 20–50 mg/ kg as a subcutaneous infusion over 8-12 hours on 3-7 days each week
• Consider oral vitamin C (200mg oral ascorbic acid) to be taken separately to food to enhance chelation

*Monitoring*
• Annual ophthalmology and audiology review including baseline
• Monitor ferritin and MRI scan to ensure response

**NB**
Desferrioxamine must be stopped and patients admitted for treatment and investigation if they develop abdominal pain and diarrhoea. *Yersinia* infection must be excluded.

Desferal can be supplied as a preprepared 'bubble' for self-administration at home. It will need to be collected from Haematology day unit every 2 weeks. Patients and or carers can be trained on day unit to be self-sufficient at using their desferrioxamine.

Desferrioxamine can be administered intravenously (iv) or for continuous infusions rather than just 12 hours depending on iron load and individual patient circumstances

In cases of cardiac iron overload it can be used in combination with deferiprone. This must only be initiated via the haematology consultant

***Deferiprone (Ferriprox)***

Deferiprone is an oral chelation agent which may be used in dual therapy with deferasirox in patients where optimum chelation is not being achieved. It can also be used as a single agent in patients who cannot tolerate desferrioxamine or deferasirox.

On initiation, regular FBC should be monitored weekly as there is a risk of drug induced neutropenia (agranulocytosis) with this medication.

Doses usually start around 25mg/kg *tds* (75mg/kg) and do not exceed 100 mg/ kg / day

**Ophthalmological Review when on Iron Chelation**

Desferrioxamine

Asymptomatic patients when starting desferrioxamine should have a baseline review including electrophysiology and retinal imaging prefably within 6 weeks of starting. They will also be seen in the medical retina clinic after the EDD for documentation of any retinopathy.

These patients should have yearly electrophysiology and psychophysic investigations

Symptomatic patients should be discussed with ophthalmology urgently as desferrioxamine can be retinotoxic. Symptoms are usually after a spell of high dose intravenous therapy. They will require urgent electrophysiology and psychophysic investigations with a full ophthalmological assessment for any abnormalities found.

Deferasirox and Deferiprone

There is less clear evidence of any retinotoxicity and so these patients should be monitored clinically and discussed with ophthalmology if there are concerns of any symptoms.

## 7. Dissemination and implementation

### 7.1 Dissemination:

Guidelines will be available on the departmental intranet page and available in paper form in the junior doctor office in haematology.

### 7.2. Implementation

Guidelines will be promoted by the haemoglobinopathy team.

## 8. Consequences of Breaching the Policy

Failing to follow this policy could lead to action under the Trust's disciplinary policy.

## 9. Monitoring compliance

The table below outlines the process for monitoring compliance with this document.

| Monitoring compliance and effectiveness table | | | | | |
|---|---|---|---|---|---|
| **Element/ Activity being monitored** | **Lead/role** | **Methodology to be used for monitoring** | **Frequency of monitoring and Reporting arrangements** | **Acting on recommendations and Leads** | **Change in practice and lessons to be shared** |
| *WMQRS peer review quality standards* | *Consultant haematologist* | *As required (every 2-3 year)* | *The lead or committee is expected to read and interrogate the report to identify deficiencies in the system and act upon them. Consider stating this responsibility in committee terms of reference.* | *Required actions will be identified and completed in a specified timeframe. Consider stating this responsibility in committee terms of reference.*<br><br>*These will be discussed at Divisional governance board* | *Required changes to practice will be identified and actioned within a specific timeframe. A lead member of the team will be identified to take each change forward where appropriate. Lessons will be shared with all the relevant stakeholders.* |

## 10. Associated documentation

Incentive Spirometry guideline for adults admitted with sickle cell crisis at risk of acute chest syndrome

## 11. References


- West Midlands Review Service – Quality Standards: Health Services for People with Haemoglobin Disorders (2018/19)

- Standards for the Clinical Care of Adults with Sickle Cell Disease in the UK 2018 (Sickle Cell Society) https://www.sicklecellsociety.org/wp-content/uploads/2018/04/Web-version-FINAL-SCS-Standards-GSM-6.4.18.pdf

- British Society Haematology : guidelines Red Cell Transfusion in Sickle Cell Disease Part I and Part II (7.11.17 and 18.11.18) https://b-s-h.org.uk/guidelines/guidelines/red-cell-transfusion-in-sickle-cell-disease-part-I/