Patient Blood Management Guidelines: Module 6

# Neonatal and Paediatrics

Quick Reference Guide

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**Publication approval**

**Australian Government**
**National Health and Medical Research Council**

The guidelines (recommendations) on pages 8–27 were approved by the Chief Executive Officer of the National Health and Medical Research Council (NHMRC) on 21 March 2016 under section 14A of the *National Health and Medical Research Council Act 1992*. In approving the guidelines (recommendations), the NHMRC considers that they meet the NHMRC standard for clinical practice guidelines. This approval is valid for a period of five years.

NHMRC is satisfied that the guidelines (recommendations) are systematically derived, based on the identification and synthesis of the best available scientific evidence, and developed for health professionals practising in an Australian health care setting.

This publication reflects the views of the authors and not necessarily the views of the Australian Government.

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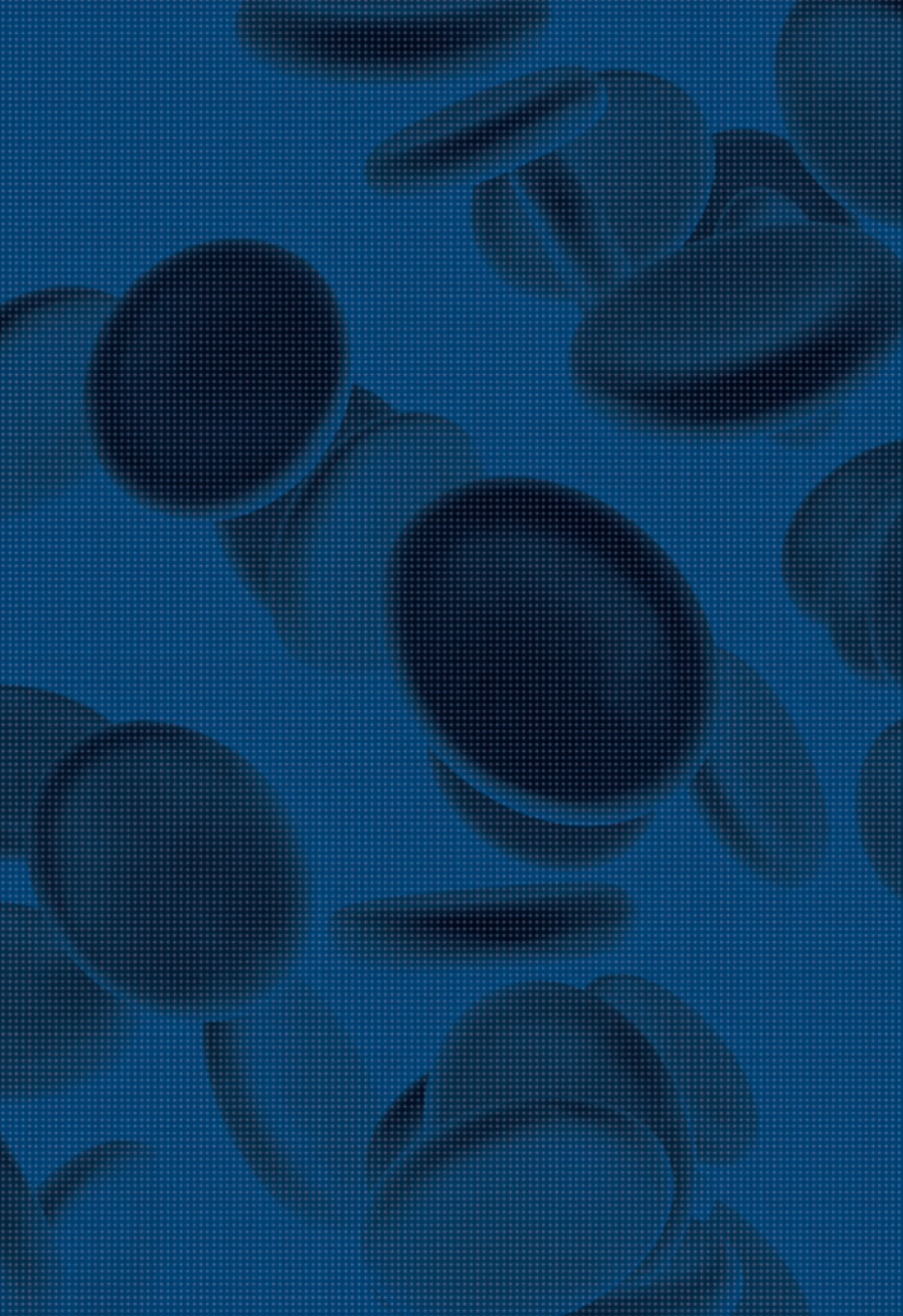

# Patient Blood Management Guidelines: Module 6 – Neonatal and Paediatrics

Development of this module was achieved through clinical input and expertise of representatives from the colleges and societies listed below, a patient blood management consultant and an independent consumer advocate (see Appendix A in the module).

**Australian and New Zealand Children's Haematology/Oncology Group**

**Australian and New Zealand Intensive Care Society**

**Australian & New Zealand Society of Blood Transfusion**

**Australian College of Children and Young People's Nurses**

**College of Intensive Care Medicine of Australia and New Zealand**

**Haematology Society of Australia & New Zealand**

**Perinatal Society of Australia and New Zealand**

**Royal Australian and New Zealand College of Obstetricians and Gynaecologists**

**Royal Australasian College of Surgeons**

**Royal Australasian College of Physicians**

**Royal College of Pathologists of Australasia**

**Thalassaemia Australia**

The National Blood Authority gratefully acknowledges these contributions. College and society endorsement of this module can be found at www.blood.gov.au


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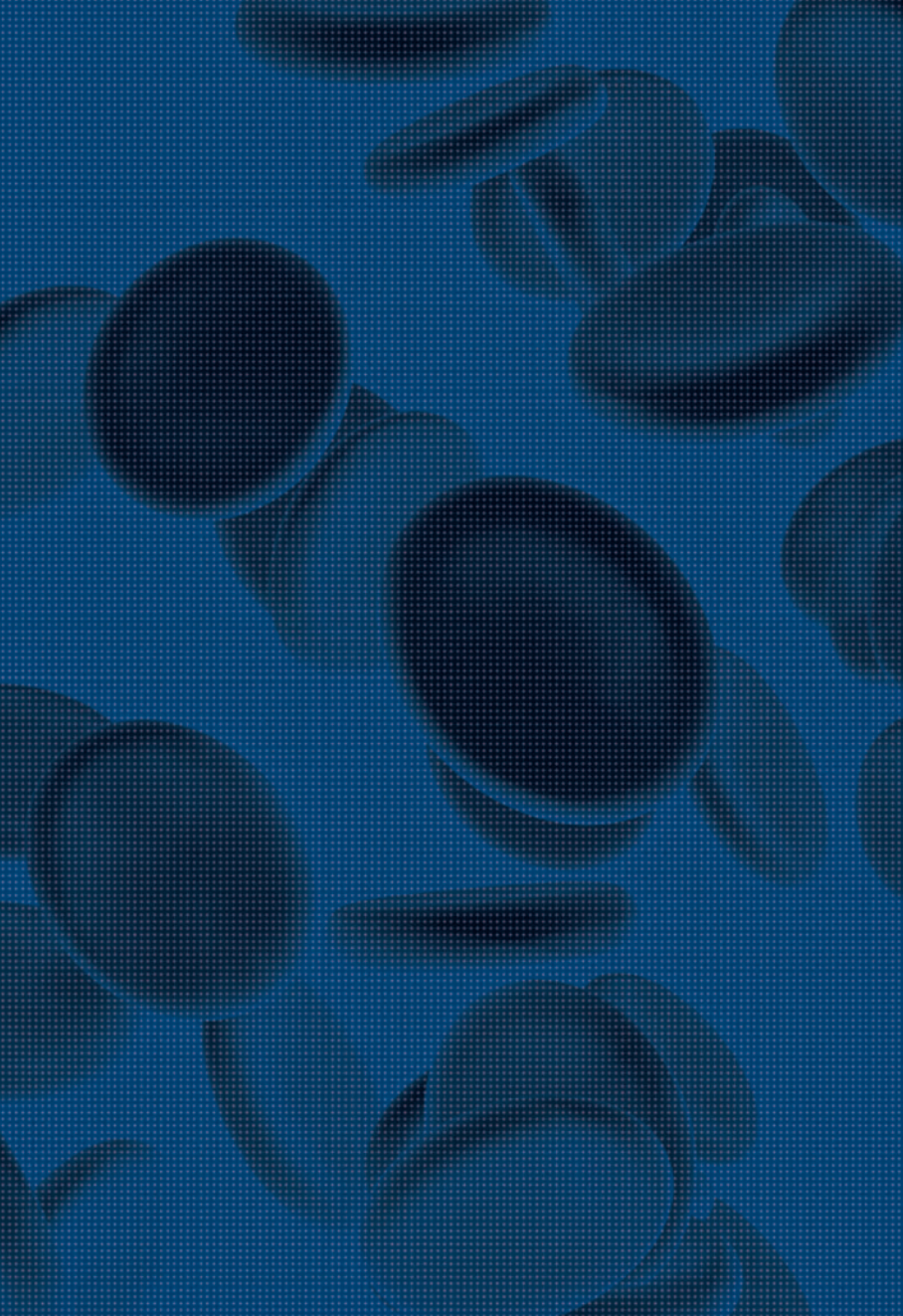
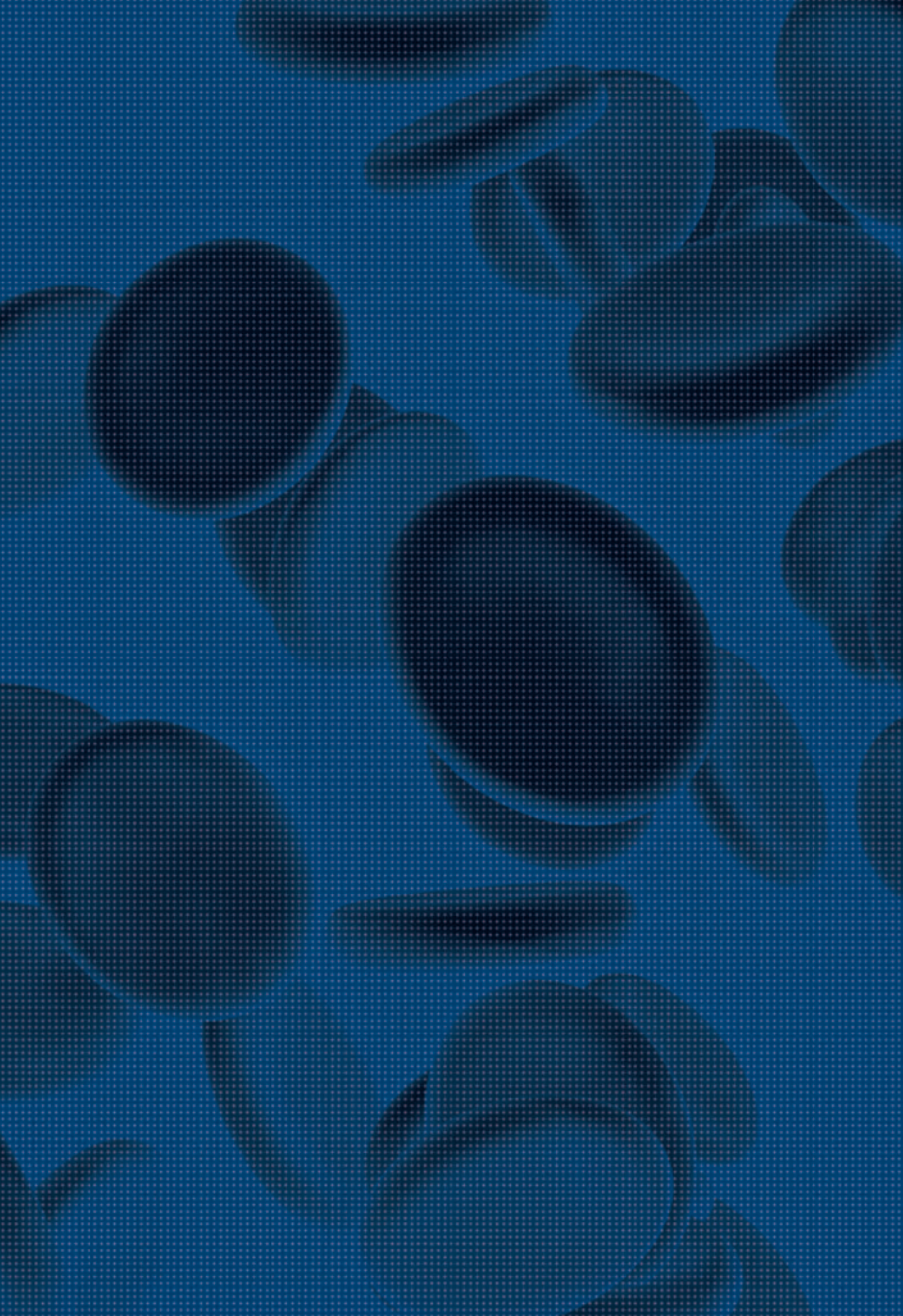


# Abbreviations and acronyms

| | |
|---|---|
| ACE | angiotensin-converting enzyme |
| AHCDO | Australian Haemophilia Centre Directors' Organisation |
| APTT | activated partial thromboplastin time |
| CMV | cytomegalovirus |
| CPAP | continuous positive airway pressure |
| CRG | Clinical/Consumer Reference Group |
| CRP | C reactive protein |
| EBV | estimated blood volume |
| EOP | expert opinion point |
| ESA | erythropoiesis stimulating agent |
| FFP | fresh frozen plasma |
| Hb | haemoglobin |
| Hct | haematocrit |
| HLA | human leucocyte antigen |
| ICS | intraoperative cell salvage |
| INR | international normalised ratio |
| IV | intravenous |
| IVIg | intravenous immunoglobulin |
| K | Kell |
| KDIGO | Kidney Disease: Improving Global Outcomes |
| MCH | mean corpuscular haemoglobin |
| MCV | mean corpuscular volume |
| MET | medical emergency team |
| MRI | magnetic resonance imaging |
| NICE | National Institute for Health and Care Excellence |
| POC | point-of-care |
| PP | practice point |
| PT | prothrombin time |
| R | recommendation |
| RBC | red blood cell |
| rFVIIa | recombinant activated factor VII |
| SD | standard deviation |
| TSAT | transferrin saturation |



# Contents

# 1. Introduction

The *Patient Blood Management Guidelines: Module 6 – Neonatal and Paediatrics*[1] (Module 6 – Neonatal and Paediatrics), is the final in a series of six modules that focus on evidence-based patient blood management. The other five modules are *Critical Bleeding/Massive Transfusion*,[2] *Perioperative*,[3] *Medical*,[4] *Critical Care*[5] and *Obstetrics and Maternity*.[6] Together, Module 2 – Perioperative[3] and Module 3 – Medical[4] cover all the patient groups addressed by the 2001 document *Clinical Practice Guidelines on the Use of Blood Components*[7] (National Health and Medical Research Council/Australasian Society of Blood Transfusion, NHMRC/ASBT).

Module 6 – Neonatal and Paediatrics[1] was developed by a Clinical/Consumer Reference Group (CRG) representing specialist colleges, organisations and societies, with the active participation of the clinical community.

This quick reference guide of Module 6[1] – Neonatal and Paediatrics includes:

- a summary of the recommendations that were developed by the CRG, based on evidence from the systematic review;
- a summary of the practice points that were developed by the CRG through consensus decision making, where the systematic review found insufficient high quality data; and
- a summary of the expert opinion points that were developed by the CRG through consensus decision making, where relevant guidance that is outside the scope of the systematic review is required.

Details of the systematic reviews used in the development of Module 6 – Neonatal and Paediatrics,[1] for which the electronic searches included articles published before 12 June 2013, are given in the technical reports[8,9] available on the National Blood Authority (NBA) website.

# 2. Development of recommendations, practice points and expert opinion points

## Recommendations

The CRG developed recommendations where sufficient evidence was available from the systematic review of the literature. The recommendations have been carefully worded to reflect the strength of the body of evidence. Each recommendation has been given a grade, using the following definitions, which were set by the NHMRC:

| | |
|---|---|
| **GRADE A** | Body of evidence can be trusted to guide practice |
| **GRADE B** | Body of evidence can be trusted to guide practice in most situations |
| **GRADE C** | Body of evidence provides some support for recommendation(s) but care should be taken in its application |
| **GRADE D** | Body of evidence is weak and recommendations must be applied with caution. |

## Practice Points

The CRG developed practice points where the systematic review found insufficient high-quality data to produce evidence-based recommendations, but the CRG felt that clinicians require guidance to ensure good clinical practice. These points are based on consensus among the members of the committee.

## Expert Opinion Points

The CRG developed expert opinion points where the CRG felt that clinicians require guidance to ensure good clinical practice that is outside the scope of the systematic review. These points are based on consensus among the members of the committee.

This quick reference guide summarises the recommendations, practice points and expert opinion points in a sequence that reflects clinical practice.

# 3. Categorisation of recommendations, practice points and expert opinion points

The following table categorises the recommendations and practice points according to different elements of patient blood management. It also identifies where to find the recommendations and practice points within this quick reference guide and Module 6 – Neonatal and Paediatrics,[1] where references are provided.

This section is followed by a series of tables giving the full recommendations and practice points for each element.

| ELEMENTS OF PATIENT BLOOD MANAGEMENT | RECOMMEN-DATION | PRACTICE POINT | EXPERT OPINION POINT | RELEVANT SECTION OF THIS QUICK REFERENCE GUIDE | RELEVENT SECTION OF MODULE 6 – NEONATAL & PAEDIATRICS |
|---|---|---|---|---|---|
| **Red Blood Cell (RBC) transfusion – indications, Hb thresholds and volume** | | | | | |
| RBC transfusion | R1 | PP1-6, 8-9, 12 | EOP8, 23-24 | 4.1.1 | 3.2.1, 3.2.2, 3.2.5-3.2.7, 4.1.2, 4.2.1 |
| RBC transfusion in chronic anaemia | R2, 4 | PP7, 10-11, 22 | EOP9 | 4.1.2 | 3.2.2, 3.2.3, 3.3.9, 4.1.2 |
| **Reducing the need for RBC transfusion** | | | | | |
| Placental transfusion | | PP32-33 | | 4.2.1 | 3.5.1 |
| Oral and/or parenteral iron | R5 | PP13-16, 24-25, 27 | EOP32-34 | 4.2.2 | 3.3.2, 3.3.4, 3.3.12, 3.3.14, 4.5.5 |
| Erythropoiesis stimulating agents (ESAs) | R3 | PP17-21, 23, 26 | | 4.2.3 | 3.3.1, 3.3.5, 3.3.7, 3.3.11, 3.3.13 |
| Reducing the need for exchange transfusion | R7 | PP34 | EOP6 | 4.2.4 | 3.5.2 |

| ELEMENTS OF PATIENT BLOOD MANAGEMENT | RECOMMEN-DATION | PRACTICE POINT | EXPERT OPINION POINT | RELEVANT SECTION OF THIS QUICK REFERENCE GUIDE | RELEVENT SECTION OF MODULE 6 – NEONATAL & PAEDIATRICS |
|---|---|---|---|---|---|
| Reducing blood loss | | | | 4.2.5 | |
| - Prevention of hypothermia | R8 | | | | 3.5.3 |
| - Antifibrinolytics | R9-11 | PP38-39 | | | 3.5.8 |
| - recombinant activated factor VII (rFVIIa) | R12 | PP40 | | | 3.5.9 |
| - Acute normovolaemic haemodilution | | PP35 | | | 3.5.5 |
| - Intraoperative cell salvage (ICS) | | PP36 | | | 3.5.6 |
| - Viscoelastic point-of-care testing | | PP37 | | | 3.5.7 |
| - Minimising phlebotomy losses | | | EOP27 | | 4.3.6 |
| - Prothrombin complex concentrates | | | EOP28-29 | | 4.4.1 |
| - Topical haemostatic agents | | | EOP30-31 | | 4.4.2 |
| **Measures to reduce coagulopathy** | | | | | |
| Platelets | | PP28, 31 | EOP4, 16-22, 25-26 | 4.3.1 | 3.4.2-3.4.4, 3.4.7, 3.4.13, 4.2.1, 4.1.5-4.1.6 |
| Fresh frozen plasma (FFP), cryoprecipitate or fibrinogen concentrate | R6 | PP29-30 | EOP1-3, 5 | 4.3.2 | 3.4.1, 3.4.4-3.4.12, 3.4.14-3.4.15 |

| ELEMENTS OF PATIENT BLOOD MANAGEMENT | RECOMMEN-DATION | PRACTICE POINT | EXPERT OPINION POINT | RELEVANT SECTION OF THIS QUICK REFERENCE GUIDE | RELEVENT SECTION OF MODULE 6 – NEONATAL & PAEDIATRICS |
|---|---|---|---|---|---|
| **Specific products for selected patients** | | | | | |
| 'Fresh' (<7 days) red blood cells | | | EOP7 | 4.4.1 | 4.1.1 |
| Irradiated blood products | | | EOP10-13 | 4.4.2 | 4.1.3 |
| Cytomegalovirus (CMV) negative blood products | | | EOP14-15 | 4.4.3 | 4.1.4 |
| **Critical bleeding** | | | | | |
| Bedside and laboratory response to critical bleeding | | PP12 | EOP35-37 | 4.5.1 | 3.2.2, 3.2.6-3.2.7, 4.6 |

CMV, cytomegalovirus; EOP, expert opinion point; ESA, Erythropoiesis stimulating agents; FFP, fresh frozen plasma; Hb, haemoglobin; ICS, intraoperative cell salvage; PP, practice point; R, recommendation; rFVIIa, recombinant activated factor VII; RBC, red blood cell

# 4. Recommendations, practice points and expert opinion points

## 4.1 Red Blood Cell (RBC) transfusion – indications, Hb thresholds and volume

### 4.1.1 RBC transfusion

| RECOMMENDATION – RBC transfusion | |
|---|---|
| **R1**<br>**GRADE C** | In paediatric patients, including those who are critically ill, a restrictive transfusion strategy is suggested.[a, b, c]<br>[a] See PP6 for guidance on a restrictive transfusion strategy.<br>[b] Higher Hb thresholds may be appropriate in very low birth weight and preterm neonates.<br>[c] See PP2, PP3 and Appendix F *(RBC transfusions in preterm infants)* of Module 6[1] (or Appendix A within this document) for guidance for preterm neonates. |

| PRACTICE POINTS – RBC transfusion | |
|---|---|
| **PP1** | In neonatal and paediatric patients, the decision to give a RBC transfusion should not be dictated by a Hb concentration alone.[a] The decision should also be based on assessment of the patient's underlying condition, anaemia-related signs and symptoms, and response to previous transfusions. Underlying conditions that may influence the decision to transfuse include acquired or congenital cardiac disease, and severe respiratory disease.<br>[a] See PP1 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] |
| **PP6** | In haemodynamically stable paediatric patients (excluding neonates), evidence from other patient groups and CRG consensus[a] suggests that, with a:<br>▪ Hb concentration <70 g/L, RBC transfusion is often appropriate. However, transfusion may not be required in well-compensated patients or where other specific therapy is available.<br>▪ Hb concentration of 70–90 g/L, RBC transfusion may be appropriate. The decision to transfuse patients should be based on the need to relieve clinical signs and symptoms of anaemia, and the patient's response to previous transfusions.<br>▪ Hb concentration >90 g/L, RBC transfusion is often unnecessary and may be inappropriate.<br>[a] See PP3 in *Patient Blood Management Guidelines: Module 4 – Critical Care*.[5] |

| | |
|---|---|
| **PP5** | For neonatal and paediatric patients, a specific procedural guideline for RBC transfusion should be used that includes the following:<br>▪ age-specific Hb reference ranges<br>▪ volume of transfusion and rate of administration<br>▪ patient monitoring during and after transfusion<br>▪ transfusion technique (e.g. use of syringe pumps)<br>▪ recognition and reporting of adverse events. |
| **PP8** | In paediatric patients less than 20 kg, calculate transfusion volume (mL) based on weight and desired Hb increment.[a, b]<br>[a] See Appendix F (*RBC transfusions in preterm infants*) of Module 6[1] (or Appendix A within this document).<br>[b] See Appendix G (*Transfusion volume calculation for neonates, infants and small children*) of Module 6[1] (or Appendix B within this document). |
| **PP9** | In most paediatric patients over 20 kg, transfusion of a single unit of RBC, followed by clinical reassessment to determine the need for further transfusion, is appropriate. This reassessment will also guide the decision on whether to retest the Hb level.[a]<br>[a] See PP2 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] |
| **PP3** | In preterm infants requiring transfusion, there is insufficient evidence to support or refute the use of either a restrictive or liberal RBC transfusion strategy. |
| **PP2** | Neonatal units should use a procedural guideline[a] for RBC transfusion in preterm infants that includes the following:<br>▪ age of infant<br>▪ age-specific Hb reference ranges<br>▪ Hb or haematocrit<br>▪ level of respiratory support<br>▪ ongoing or anticipated red cell loss<br>▪ nutritional status.<br>[a] See Appendix F (*RBC transfusions in preterm infants*) of Module 6[1] (or Appendix A within this document). |

| | |
|---|---|
| **PP4** | In neonatal patients, calculate transfusion volume (mL) based on weight and desired Hb increment.[a, b]<br>[a] See Appendix F (*RBC transfusions in preterm infants*) of Module 6[1] (or Appendix A within this document).<br>[b] See Appendix G (*Transfusion volume calculation for neonates, infants and small children*) of Module 6[1] (or Appendix B within this document). |
| **PP12** | In neonatal and paediatric patients with critical bleeding requiring massive transfusion, use a critical bleeding protocol.[a] A template protocol is provided within the module.[b]<br>[a] The use of the word 'protocol' is not strictly prescriptive.<br>[b] The template given in Appendix K (*Critical bleeding protocol*) of Module 6[1] (or Appendix F within this document) is intended for local adaptation. |
| EXPERT OPINION POINT – Kell antigen system | |
| **EOP8** | Where possible, K-negative RBC should be selected for transfusion for all females of childbearing potential who are K negative or whose K antigen status is unable to be determined prior to transfusion. This includes fetal transfusion. |
| EXPERT OPINION POINTS – fetal transfusion | |
| **EOP23** | Management of pregnancies at risk of fetal anaemia or thrombocytopenia should be undertaken in facilities with appropriate expertise in ultrasound imaging and invasive fetal interventions, and that have access to specific blood products and neonatal intensive care. |
| **EOP24** | Pregnancies at risk of fetal anaemia should be assessed by Doppler ultrasound of the fetal middle cerebral artery peak systolic velocity, to determine whether fetal blood sampling and intrauterine transfusion are necessary. |

CRG, Clinical/Consumer Reference Group; EOP, expert opinion point; Hb, haemoglobin; K, Kell; PP, practice point; R, recommendation; RBC, red blood cell

### 4.1.2 RBC transfusion in chronic anaemia

| RECOMMENDATION – sickle cell disease (RBC transfusion) | |
|---|---|
| **R2**<br>**GRADE A** | In children and adolescents with sickle cell disease who have been assessed to be at increased risk of stroke,[a] a program of prophylactic RBC transfusions should be used in order to reduce stroke occurrence.[b]<br>[a] Assessed by transcranial Doppler ultrasonography[10] and MRI.[11]<br>[b] See PP11 for methods of assessment. |

| PRACTICE POINT – sickle cell disease (RBC transfusion) | |
|---|---|
| **PP11** | Children and adolescents with sickle cell disease should be assessed for stroke risk using both transcranial Doppler ultrasonography[10] and MRI.[11] |

| RECOMMENDATION – sickle cell disease (hydroxyurea) | |
|---|---|
| **R4**<br>**GRADE B** | In paediatric patients with sickle cell disease, hydroxyurea should not be given for the primary purpose of reducing transfusion incidence.[a, b]<br>[a] Although hydroxyurea reduces transfusion incidence, it may not be the optimal treatment for prevention of stroke.<br>[b] See R2 and PP22. |

| PRACTICE POINT – sickle cell disease (hydroxyurea) | |
|---|---|
| **PP22** | In paediatric patients over 9 months of age with sickle cell disease, hydroxyurea should be offered to reduce vaso-occlusive pain crises and acute chest syndromes. |

| PRACTICE POINT – beta thalassaemia (RBC transfusion) | |
|---|---|
| **PP7** | In paediatric patients with beta thalassaemia, the evidence does not support any change to the current practice of maintaining a pretransfusion Hb concentration of 90–100 g/L.[a]<br>[a] See PP23 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] |

| PRACTICE POINT – infants, children and adolescents (RBC transfusion) | |
|---|---|
| **PP10** | In paediatric patients over 20 kg who are chronically transfused (e.g. haemoglobinopathies or bone marrow failure syndromes) a single-unit approach may not be appropriate. Instead, calculation of the transfusion volume (mL) should be based on weight and desired Hb increment. |
| **EXPERT OPINION POINT – Kell antigen system** | |
| **EOP9** | In both male and female chronically transfused patients, RBC should be selected to match RhD, C/c, E/e and K antigen status. |

EOP, expert opinion point; Hb, haemoglobin; K, Kell; MRI, magnetic resonance imaging; PP, practice point; R, recommendation; RBC, red blood cell

## 4.2 Reducing the need for RBC transfusion

### 4.2.1 Placental transfusion

| PRACTICE POINTS – preterm and term infants (placental transfusion) | |
|---|---|
| **PP32** | In preterm infants, deferring cord clamping for between 30 seconds and 3 minutes may reduce transfusion volume and incidence, and incidence of intraventricular haemorrhage. However, the effect of this practice on other outcomes (death, major morbidity and neurodevelopmental outcomes) is uncertain or unknown, particularly in extremely preterm infants (e.g. <28 weeks) and in those who require active resuscitation. |
| **PP33** | In term infants, deferring cord clamping for at least 1 minute is likely to reduce the risk of iron deficiency at 3–6 months. This intervention should be considered in infants who do not require active resuscitation, provided that access to phototherapy for jaundice is available.[a]<br>[a] See McDonald et al (2013).[12] |

PP, practice point

### 4.2.2 Oral and/or parenteral iron

| RECOMMENDATION – surgical (oral and/or parenteral iron) | |
|---|---|
| **R5**<br>**GRADE C** | In surgical paediatric patients with or at risk of iron deficiency anaemia, preoperative iron therapy is recommended.[a]<br>[a] See R4 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] |

| PRACTICE POINTS – surgical (oral and/or parenteral iron) | |
|---|---|
| **PP24** | In neonatal and paediatric surgical patients in whom substantial blood loss is anticipated, preoperative anaemia and iron deficiency[a] should be identified, evaluated and managed to minimise RBC transfusion.[b]<br>[a] Iron deficiency can be present with a normal Hb.<br>[b] See Appendix H (*Paediatric haemoglobin assessment and optimisation template*) of Module 6[1] (or Appendix C within this document) for further information on the optimal dosing strategy. |
| **PP25** | To implement PP24, patients should be evaluated as early as possible so that scheduling of surgery can be coordinated with optimisation of the patient's Hb and iron stores. |

| PRACTICE POINT – preterm and low birth weight infants (oral and/or parenteral iron) | |
|---|---|
| **PP13** | Preterm and low birth weight infants should receive iron supplementation as necessary to achieve the recommended nutrient intake. However, routine supplementation in excess of the recommended nutrient intake, to reduce transfusion incidence, is not supported. |

| PRACTICE POINTS – infants, children and adolescents (oral and/or parenteral iron) | |
|---|---|
| **PP14** | Infants and children should receive sufficient dietary iron to achieve the adequate intake or recommended daily intake. If the adequate intake or recommended daily intake cannot be met by dietary means, iron supplementation is advised. |
| **PP15** | Infants and children in populations at high risk[a] of iron deficiency should be screened for this condition.[b]<br>[a] See Domellof et al (2014)[13] and Pottie et al (2011).[14]<br>[b] See Section 3.6 of Module 6.[1] |

| | |
|---|---|
| **PP16** | Infants and children with iron deficiency should be treated with iron supplements and dietary modifications. |

| PRACTICE POINT – critically ill (oral and/or parenteral iron) | |
|---|---|
| **PP27** | Critically ill paediatric patients should receive iron supplementation as necessary to achieve the recommended nutrient intake. |

| EXPERT OPINION POINTS – iron therapy | |
|---|---|
| **EOP32** | From 6 months of age, all infants and children should receive iron-rich foods. |
| **EOP33** | Cow's milk should not be given to infants before 12 months of age; from 12 months of age, cow's milk intake should not exceed 500 mL per day. |
| **EOP34** | IV iron should be administered according to a protocol relevant to the specific product being used:[a]<br>▪ IV iron formulations have different iron concentrations, maximum doses, dilutions and rates of administration; they are not interchangeable with regard to dose, dilution and rates of administration<br>▪ IV iron formulations should only ever be administered in an appropriate health-care setting with medical personnel and resuscitation facilities on site.<br>[a] See Appendix I (*Intravenous iron*) of Module 6[1] (or Appendix D within this document) for further information. |

EOP, expert opinion point; Hb, haemoglobin; IV, intravenous; PP, practice point; R, recommendation

### 4.2.3 Erythropoiesis stimulating agents (ESAs)

| RECOMMENDATION – preterm and low birth weight infants (ESAs with or without iron) | |
|---|---|
| **R3**<br>**GRADE C** | In preterm infants with low birth weight (<2500 g), the *routine* use of ESAs is not advised. |

## PRACTICE POINT – cancer (ESAs with or without iron)

| | |
|---|---|
| **PP17** | In paediatric patients receiving chemotherapy, the *routine* use of ESAs is not advised.<br>The use of ESAs may reduce transfusion incidence; however, the studies are underpowered to determine their effect on mortality and thromboembolic events, which are increased in the adult population.[a]<br>[a] See R2 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] |

## PRACTICE POINTS – kidney disease (ESAs with or without iron)

| | |
|---|---|
| **PP18** | In paediatric patients with chronic kidney disease, ESA therapy to achieve a low to intermediate Hb target may be used to avoid RBC transfusion, after consideration of risks and benefits for the individual patient.[a, b, c]<br>[a] See R4 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4]<br>[b] The KDIGO guidelines[15] recommend a Hb target of 110–120 g/L for paediatric patients and state that individualisation of ESA therapy is reasonable because some patients may have improvements in quality of life at higher Hb concentration.<br>[c] The NICE guidelines[16] recommend a Hb target of 100–120 g/L for children aged 2 years and older, and 95–115 g/L for children younger than 2 years of age (reflecting the lower normal range in that age group). |
| **PP19** | In adult patients with chronic kidney disease, ESA therapy to achieve a Hb target of >130 g/L is not recommended because of increased morbidity; therefore, it is sensible to apply this limit to paediatric patients.[a]<br>[a] See R6 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] |
| **PP20** | ESA use is less effective in patients with chronic kidney disease who have absolute or functional iron deficiency.[a]<br>[a] See PP13 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] |
| **PP21** | Where ESAs are indicated for the treatment or prevention of anaemia in neonatal and paediatric patients, they should be combined with iron therapy. |

## PRACTICE POINT – surgical (ESAs with or without iron)

| | |
|---|---|
| **PP23** | In neonatal and paediatric surgical patients, an ESA should only be prescribed in consultation with a paediatric haematologist, and should be combined with iron therapy. |

| PRACTICE POINT – critically ill (ESAs with or without iron) | |
|---|---|
| **PP26** | In critically ill paediatric patients with anaemia, ESAs should not be *routinely* used.[a]<br>[a] This point is based on the lack of effect of ESAs on mortality in critically ill adult patients. See R2 in *Patient Blood Management Guidelines: Module 4 – Critical Care*.[5] |

ESA, erythropoiesis stimulating agent; Hb, haemoglobin; KDIGO, Kidney Disease: Improving Global Outcomes; NICE, National Institute for Health and Care Excellence; PP, practice point; R, recommendation; RBC, red blood cell

### 4.2.4 Reducing the need for exchange transfusion

| RECOMMENDATION – haemolytic disease (IVIg) | |
|---|---|
| **R7**<br>**GRADE B** | In neonates with haemolytic disease of the fetus and newborn, the use of IVIg is not recommended. |

| PRACTICE POINT – haemolytic disease (IVIg) | |
|---|---|
| **PP34** | Neonates at risk of haemolytic disease of the fetus and newborn should be promptly assessed after birth. Those at high risk of severe jaundice should receive intensive phototherapy. |

| EXPERT OPINION POINT - haemolytic disease (IVIg) | |
|---|---|
| **EOP6** | In maternity patients with a fetus affected by haemolytic disease of the fetus and newborn who is at high risk of early fetal hydrops or death, a course of weekly IVIg should be considered. |

EOP, expert opinion point; IVIg, intravenous immunoglobulin; PP, practice point; R, recommendation

### 4.2.5 Reducing blood loss

*Prevention of hypothermia*

| RECOMMENDATION – surgical (prevention of hypothermia) | |
|---|---|
| **R8**<br>**GRADE B** | In paediatric patients undergoing surgery, measures to prevent hypothermia should be used.[a]<br>[a] See R12 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] |

R, recommendation

*Antifibrinolytics*

## RECOMMENDATIONS – surgical (antifibrinolytics)

**R9**

**GRADE C**

In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, the use of antifibrinolytics is suggested.[a, b, c]

[a] Although there is evidence of a reduction in transfusion, there is insufficient evidence to determine the risk of thromboembolic complications.

[b] Tranexamic acid in this context is approved in Australia. The use of aprotinin in this context is considered off label in Australia. Epsilon-aminocaproic acid is not licensed for use in Australia.

[c] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information.

**R10**

**GRADE C**

In paediatric patients undergoing surgery for scoliosis in whom substantial blood loss is anticipated, the use of antifibrinolytics may be considered.[a, b]

[a] Tranexamic acid in this context is approved in Australia. The use of aprotinin in this context is considered off label in Australia. Epsilon-aminocaproic acid is not licensed for use in Australia.

[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information.

**R11**

**GRADE C**

In paediatric patients undergoing craniofacial surgery in whom substantial blood loss is anticipated, the use of antifibrinolytics may be considered.[a, b]

[a] Tranexamic acid in this context is approved in Australia. The use of aprotinin in this context is considered off label in Australia. Epsilon-aminocaproic acid is not licensed for use in Australia.

[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information.

## PRACTICE POINTS – surgical (antifibrinolytics)

**PP38**

In acutely bleeding critically ill paediatric trauma patients, tranexamic acid should be administered within 3 hours of injury.[a, b]

[a] See R3 in *Patient Blood Management Guidelines: Module 4 – Critical Care*.[5]

[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information.

| | |
|---|---|
| **PP39** | In paediatric trauma patients aged under 12 years, a tranexamic acid dose of 15 mg/kg (maximum 1000 mg) infused intravenously over 10 minutes, followed by 2 mg/kg/hour (maximum 125 mg/hour) until bleeding is controlled or for up to 8 hours is suggested.[a, b]<br>[a] See the template given in Appendix K (*Critical bleeding protocol*) of Module 6[1] (or Appendix F within this document), which is intended for local adaptation.<br>[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. |

PP, practice point; R, recommendation

### *Recombinant activated factor VII (rFVIIa)*

| RECOMMENDATION – surgical (rFVIIa) | |
|---|---|
| **R12**<br>**GRADE C** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, the *routine* use of rFVIIa is not recommended. |

| PRACTICE POINT – surgical (rFVIIa) | |
|---|---|
| **PP40** | The administration of rFVIIa may be considered in the perioperative patient with life-threatening haemorrhage after conventional measures, including surgical haemostasis, use of antifibrinolytics and appropriate blood component therapy have failed.[a, b]<br>[a] rFVIIa is not licensed for this use; its use should only be considered in exceptional circumstances.<br>[b] See R22 and PP20 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] |

PP, practice point; R, recommendation; rFVIIa, recombinant activated factor VII

### *Acute normovolaemic haemodilution*

| PRACTICE POINT – surgical (acute normovolaemic haemodilution) | |
|---|---|
| **PP35** | In paediatric patients, acute normovolaemic haemodilution has not been shown to reduce transfusion or improve clinical outcomes. However, if acute normovolaemic haemodilution is used, it requires a local procedural guideline that addresses patient selection, vascular access, volume of blood withdrawn, choice of replacement fluid, blood storage and handling, and timing of reinfusion. |

PP, practice point

*Intraoperative cell salvage (ICS)*

| PRACTICE POINT – surgical (intraoperative cell salvage) | |
|---|---|
| **PP36** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, intraoperative cell salvage may be considered. If intraoperative cell salvage is used, it requires a local procedural guideline that should include patient selection, use of equipment and reinfusion. All staff operating cell salvage devices should receive appropriate training, to ensure knowledge of the technique and proficiency in using it. |

PP, practice point

*Viscoelastic point-of-care testing*

| PRACTICE POINT – surgical (viscoelastic point-of-care testing) | |
|---|---|
| **PP37** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, viscoelastic point-of-care testing may be considered. |

PP, practice point

### *Minimising phlebotomy losses*

| EXPERT OPINION POINT – strategies for minimisation of blood loss | |
|---|---|
| **EOP27** | Strategies to safely minimise phlebotomy losses should be used for all neonatal and paediatric patients. Such strategies may include (where safe and feasible):<br>▪ use of 'as-needed' rather than routine sampling<br>▪ meticulous avoidance of blood overdraw<br>▪ return of void volumes to sampling lines<br>▪ use of closed inline sampling devices<br>▪ judicious use and 'on-time' removal of sampling lines<br>▪ optimal sampling technique and sample handling to minimise rejection of samples by laboratory<br>▪ laboratory equipment that uses the smallest possible sample volumes<br>▪ use of non-invasive techniques and point-of-care devices<br>▪ audit compliance and cumulative phlebotomy losses in selected groups of patients at regular intervals. |

EOP, expert opinion point

### *Prothrombin complex concentrates*

| EXPERT OPINION POINTS – prothrombin complex concentrates | |
|---|---|
| **EOP28** | Prothrombin complex concentrates may be considered in neonatal and paediatric patients undergoing urgent surgery who are receiving vitamin K antagonists.[17] |
| **EOP29** | Prothrombin complex concentrates may be considered to treat bleeding in paediatric patients at high risk of volume overload (e.g. those who have undergone cardiac surgery on cardiopulmonary bypass). |

EOP, expert opinion point

*Topical haemostatic agents*

| EXPERT OPINION POINTS – topical haemostatic agents | |
|---|---|
| **EOP30** | Topical haemostatic agents may be considered in neonatal and paediatric surgical patients as an adjuvant to control bleeding. |
| **EOP31** | The use of topical haemostatic agents should adhere to the manufacturer's instructions and safety information. |

EOP, expert opinion point

## 4.3 Measures to reduce coagulopathy

### 4.3.1 Platelets

| PRACTICE POINTS – platelet transfusion | |
|---|---|
| **PP28** | In neonatal and paediatric patients, the decision to transfuse platelets should take into account the potential risks and benefits. The decision should be based not only on laboratory investigations but also on assessment of the patient's clinical condition. Factors that may influence the decision include active bleeding, medications affecting platelet function and coagulation status, and congenital and acquired bleeding disorders. |
| **PP31** | In patients undergoing chemotherapy and haematopoietic stem cell transplantation, the recommended strategy for prophylactic use of platelets is transfusion at a platelet count of $<10 \times 10^9$/L in the absence of risk factors, and at $<20 \times 10^9$/L in the presence of risk factors (e.g. fever, minor bleeding).[a]<br>[a] See R8 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] |

| EXPERT OPINION POINT – surgical (platelet transfusion) | |
|---|---|
| **EOP4** | In general, neonatal and paediatric patients with a platelet count $\geq 50 \times 10^9$/L can undergo invasive procedures without any serious bleeding; however, lower platelet counts may be tolerated.[a]<br>[a] See PP17 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] |

| EXPERT OPINION POINTS – fetal transfusion | |
|---|---|
| **EOP25** | Pregnant women who have had a prior pregnancy with fetal or neonatal intracranial haemorrhage or thrombocytopenia due to fetal and neonatal alloimmune thrombocytopenia should be managed with IVIg.[18] |
| **EOP26** | Fetal blood sampling should be considered to assess response to IVIg in those who have had a previous child with intracranial haemorrhage due to fetal and neonatal alloimmune thrombocytopenia. The risk of fetal blood sampling should be balanced against the risk of bleeding due to suboptimal IVIg response. |

| EXPERT OPINION POINTS – use of human platelet antigen-matched platelets | |
|---|---|
| **EOP16** | For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia:<br>▪ urgent platelet transfusion should be given if platelets are below $30 \times 10^9$/L in a term infant or below $50 \times 10^9$/L in a preterm infant, even in the absence of clinically significant bleeding<br>▪ if there is active bleeding, a higher threshold should be considered ($100 \times 10^9$/L for intracranial bleeding, and $50 \times 10^9$/L for other sites of bleeding)<br>▪ in all cases, a paediatric haematologist should be consulted. |
| **EOP17** | For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia, platelet count response to transfusion should be checked within 12 hours. |
| **EOP18** | For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia, random donor platelets should be used if antigen-matched platelets are not immediately available. Continued use of random donor platelets is acceptable if antigen-matched platelets cannot be obtained. Because of short survival of random donor platelets, repeated transfusion is likely to be needed. |
| **EOP19** | For neonates with fetal and neonatal alloimmune thrombocytopenia, IVIg may be considered.[18] |

| EXPERT OPINION POINTS – use of human leukocyte antigen-matched platelets | |
|---|---|
| **EOP20** | For neonatal and paediatric patients with platelet refractoriness attributable to non-immune causes such as splenomegaly or infection, fresh, ABO-compatible, single-donor apheresis platelets may improve platelet increment. |
| **EOP21** | If the cause of platelet refractoriness is not obvious, investigation should include screening for HLA antibodies. HLA-matched platelets should be used if an HLA antibody is detected.<br>If the HLA antibody screen is negative or there is a poor response to HLA-matched platelets, screening for human platelet antigen antibodies should be undertaken, followed by use of human platelet antigen-matched platelets if positive. |
| **EOP22** | In patients with inherited platelet disorders such as Bernard Soulier Syndrome and Glanzmann's thrombasthenia, platelet transfusions should be avoided if possible, to reduce the patient's risk of alloimmunisation. If platelet transfusion is unavoidable the patient should receive HLA-matched platelets. |

EOP, expert opinion point; HLA, human leucocyte antigen; IVIg, intravenous immunoglobulin; PP, practice point; R, recommendation

### 4.3.2 Fresh frozen plasma (FFP), cryoprecipitate or fibrinogen concentrate

| RECOMMENDATION – surgical (Fresh frozen plasma) | |
|---|---|
| **R6**<br>**GRADE C** | In neonatal and paediatric patients undergoing cardiac surgery, the *routine* use of an FFP-based pump prime solution is not recommended, because it offers no advantages over an albumin-based solution in relation to postoperative blood loss, or perioperative transfusion requirements. |

| PRACTICE POINT – Fresh frozen plasma (FFP), cryoprecipitate or fibrinogen concentrate | |
|---|---|
| **PP29** | In neonatal and paediatric patients, the decision to transfuse FFP, cryoprecipitate or fibrinogen concentrate should take into account the potential risks and benefits. The decision should be based not only on laboratory investigations but also on assessment of the patient's clinical condition. Factors that may influence the decision include active bleeding, medications affecting coagulation status, and congenital and acquired bleeding disorders. |

## PRACTICE POINT – Fresh frozen plasma (FFP)

| | |
|---|---|
| **PP30** | For guidance on the use of FFP in specific patient groups, refer to:[a]<br>▪ *Patient Blood Management Guidelines: Module 1 – Critical Bleeding/Massive Transfusion (2011)*[2]<br>▪ *Patient Blood Management Guidelines: Module 2 – Perioperative (2012)*[3]<br>▪ *Warfarin Reversal: Consensus Guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis (2004)*[19]<br>▪ AHCDO guidelines for patients with specific factor deficiencies (www.ahcdo.org.au)<br>▪ *Guidelines for the Use of Fresh-Frozen Plasma, Cryoprecipitate and Cryosupernatant (2004).*[20]<br>[a] See PP17 from *Patient Blood Management Guidelines: Module 3 – Medical.*[4] |

## EXPERT OPINION POINTS – surgical (Fresh frozen plasma)

| | |
|---|---|
| **EOP1** | In neonatal and paediatric patients undergoing surgery, FFP is only indicated for treatment of active bleeding where coagulopathy is a contributing factor. Its use should be guided by clinical assessment, supplemented by point-of-care or laboratory testing. |
| **EOP2** | In general, neonatal and paediatric patients with an INR ≤2 can undergo invasive procedures without any serious bleeding; however, higher INRs may be tolerated.[a]<br>[a] See PP17 in *Patient Blood Management Guidelines: Module 2 – Perioperative.*[3] |

## EXPERT OPINION POINT – surgical (cryoprecipitate)

| | |
|---|---|
| **EOP3** | Cryoprecipitate should be used to treat active bleeding when the fibrinogen level is <1.5 g/L. A target level of 2 g/L may be appropriate in certain situations (e.g. when critical bleeding is occurring or anticipated).[a]<br>[a] The template given in Appendix K (*Critical bleeding protocol*) of Module 6[1] (or Appendix F within this document) is intended for local adaptation. |

## EXPERT OPINION POINT – surgical (platelet transfusion)

| | |
|---|---|
| **EOP5** | Specialist guidelines or haematology advice should be sought for at-risk patients undergoing intracranial, intraocular and neuraxial procedures, and for patients with severe thrombocytopenia or coagulopathy. |

AHCDO, Australian Haemophilia Centre Directors' Organisation; EOP, expert opinion point; INR, international normalised ratio; FFP, fresh frozen plasma; PP, practice point; R, recommendation

## 4.4 Specific products for selected patients

### 4.4.1 'Fresh' (<7 days) red blood cells

| EXPERT OPINION POINT – 'fresh' RBCs in fetal, neonatal and paediatric patients | |
|---|---|
| **EOP7** | 'Fresh' (<7 days) RBCs are not advocated for routine use, but may be considered in the following clinical situations:<br>▪ intrauterine transfusion (<5 days, if available)<br>▪ large-volume transfusion (>25 mL/kg)<br>▪ exchange transfusion<br>▪ cardiac surgery<br>▪ transfusion-dependent chronic anaemia (RBCs <14 days)<br>▪ where irradiated blood products are used. |

EOP, expert opinion point; RBC, red blood cell

### 4.4.2 Irradiated cellular blood products

| EXPERT OPINION POINTS – irradiated cellular blood products | |
|---|---|
| **EOP10** | Irradiated cellular blood products (RBCs and platelets) are used to prevent transfusion-associated graft-versus-host disease, and are indicated for:<br>▪ intrauterine transfusion, and recipients of prior intrauterine transfusion up to 6 months of age<br>▪ suspected or known severe congenital T-cell immunodeficiency (e.g. severe combined immunodeficiency)<br>▪ severe acquired T-cell dysfunction, related to either disease or drug therapy (see published guidelines)[21-22]<br>▪ human leukocyte antigen-matched cellular blood products (RBCs, platelets and granulocytes).<br>They may also be considered for:<br>▪ neonatal exchange transfusion, provided this does not unduly delay transfusion<br>▪ very low birth weight neonates, especially extremely preterm (<28 weeks) or extremely low birth weight infants<br>▪ certain patients undergoing chemotherapy (depending on degree of immunosuppression). |

| | |
|---|---|
| **EOP11** | Stem cells must not be irradiated. |
| **EOP12** | Hyperkalaemia may occur when large volumes of irradiated blood are transfused. In patients at risk, irradiated blood should be as fresh as possible (<7 days) and used within 24 hours of irradiation. |
| **EOP13** | Patients at high risk of transfusion-associated graft-versus-host disease should be informed of the need for irradiated blood products. Also, alerts should be incorporated in the information systems of the health service and transfusion laboratory. |

EOP, expert opinion point; RBC, red blood cell

### 4.4.3 Cytomegalovirus (CMV) – negative blood products

| EXPERT OPINION POINTS – CMV-negative cellular products | |
|---|---|
| **EOP14** | CMV-negative products may be considered in the following situations:<br>▪ intrauterine transfusion<br>▪ preterm neonates (up to 28 days after expected date of delivery)<br>▪ patients with severe combined immunodeficiency who are CMV negative<br>▪ stem cell transplantation where both donor and recipient are known to be CMV negative<br>▪ granulocyte transfusions for recipients who are CMV seronegative, or whose status is unknown.<br>CMV-negative products are generally not required in other clinical settings. |
| **EOP15** | In urgent situations, if CMV-seronegative blood components are not available, CMV-unscreened leucodepleted components should be used to avoid delays. |

CMV, cytomegalovirus; EOP, expert opinion point

## 4.5 Critical Bleeding

### 4.5.1 Bedside and laboratory response to critical bleeding

| PRACTICE POINT – critical bleeding protocol | |
|---|---|
| **PP12** | In neonatal and paediatric patients with critical bleeding requiring massive transfusion, use a critical bleeding protocol.[a] A template protocol is provided within the module.[b]<br>[a] The use of the word 'protocol' is not strictly prescriptive.<br>[b] The template given in Appendix K *(Critical bleeding protocol)* of Module 6[1] (or Appendix F within this document) is intended for local adaptation. |
| **EXPERT OPINION POINTS – critical bleeding protocol** | |
| **EOP35** | Institutions that provide care for neonates and paediatric patients should have a critical bleeding protocol specific to such patients. |
| **EOP36** | The critical bleeding protocol should outline the essential steps (including coordination and communication) to rapidly and effectively manage a patient who is at risk of or undergoing critical bleeding. |
| **EOP37** | The critical bleeding protocol should include weight adjustments to guide blood product supply and administration. The clinician, in consultation with the haematologist or transfusion specialist, should tailor the type, volume and order of products given to the clinical circumstances. |

EOP, expert opinion point; PP, practice point

# 5. Recommendations, practice points and expert opinion points with links to clinical condition

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **Red blood cell (RBC) transfusion – indications, Hb thresholds and volume** *RBC transfusion* | | | | | | | | | |
| **R1** **GRADE C** | In paediatric patients, including those who are critically ill, a restrictive transfusion strategy is suggested.[a, b, c]<br>[a] See PP6 for guidance on a restrictive transfusion strategy.<br>[b] Higher Hb thresholds may be appropriate in very low birth weight and preterm neonates.<br>[c] See PP2, PP3 and Appendix F *(RBC transfusions in preterm infants)* of Module 6[1] (or Appendix A within this document) for guidance for preterm neonates. | | | ✓ | ✓ | ✓ | | | ✓ |
| **PP1** | In neonatal and paediatric patients, the decision to give a RBC transfusion should not be dictated by a Hb concentration alone.[a] The decision should also be based on assessment of the patient's underlying condition, anaemia-related signs and symptoms, and response to previous transfusions. Underlying conditions that may influence the decision to transfuse include acquired or congenital cardiac disease, and severe respiratory disease.<br>[a] See PP1 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| **PP6** | In haemodynamically stable paediatric patients (excluding neonates), evidence from other patient groups and CRG consensus[a] suggests that, with a:<br>▪ Hb concentration <70 g/L, RBC transfusion is often appropriate. However, transfusion may not be required in well-compensated patients or where other specific therapy is available.<br>▪ Hb concentration of 70–90 g/L, RBC transfusion may be appropriate. The decision to transfuse patients should be based on the need to relieve clinical signs and symptoms of anaemia, and the patient's response to previous transfusions.<br>▪ Hb concentration >90 g/L, RBC transfusion is often unnecessary and may be inappropriate.<br>[a] See PP3 in *Patient Blood Management Guidelines: Module 4 – Critical Care*.[5] | | | ✓ | ✓ | ✓ | | | ✓ |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **PP5** | For neonatal and paediatric patients, a specific procedural guideline for RBC transfusion should be used that includes the following:<br>▪ age-specific Hb reference ranges<br>▪ volume of transfusion and rate of administration<br>▪ patient monitoring during and after transfusion<br>▪ transfusion technique (e.g. use of syringe pumps)<br>▪ recognition and reporting of adverse events. | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| **PP8** | In paediatric patients less than 20 kg, calculate transfusion volume (mL) based on weight and desired Hb increment.[a, b]<br>[a] See Appendix F (*RBC transfusions in preterm infants*) of Module 6[1] (or Appendix A within this document).<br>[b] See Appendix G (*Transfusion volume calculation for neonates, infants and small children*) of Module 6[1] (or Appendix B within this document). | | | ✓ | ✓ | ✓ | | | |
| **PP9** | In most paediatric patients over 20 kg, transfusion of a single unit of RBC, followed by clinical reassessment to determine the need for further transfusion, is appropriate. This reassessment will also guide the decision on whether to retest the Hb level.[a]<br>[a] See PP2 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] | | | ✓ | ✓ | ✓ | ✓ | | ✓ |
| **PP3** | In preterm infants requiring transfusion, there is insufficient evidence to support or refute the use of either a restrictive or liberal RBC transfusion strategy. | ✓ | | | | | | | |
| **PP2** | Neonatal units should use a procedural guideline[a] for RBC transfusion in preterm infants that includes the following:<br>▪ age of infant<br>▪ age-specific Hb reference ranges<br>▪ Hb or haematocrit<br>▪ level of respiratory support<br>▪ ongoing or anticipated red cell loss<br>▪ nutritional status.<br>[a] See Appendix F (*RBC transfusions in preterm infants*) of Module 6[1] (or Appendix A within this document). | ✓ | | ✓ | ✓ | | | | |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **PP4** | In neonatal patients, calculate transfusion volume (mL) based on weight and desired Hb increment.[a, b]<br>[a] See Appendix F (*RBC transfusions in preterm infants*) of Module 6[1] (or Appendix A within this document).<br>[b] See Appendix G (*Transfusion volume calculation for neonates, infants and small children*) of Module 6[1] (or Appendix B within this document). | ✓ | | | | | | | |
| **PP12** | In neonatal and paediatric patients with critical bleeding requiring massive transfusion, use a critical bleeding protocol.[a] A template protocol is provided within the module.[b]<br>[a] The use of the word 'protocol' is not strictly prescriptive.<br>[b] The template given in Appendix K (*Critical bleeding protocol*) of Module 6[1] (or Appendix F within this document) is intended for local adaptation. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **EOP8** | Where possible, K-negative RBC should be selected for transfusion for all females of childbearing potential who are K negative or whose K antigen status is unable to be determined prior to transfusion. This includes fetal transfusion. | ✓ | | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| **EOP23** | Management of pregnancies at risk of fetal anaemia or thrombocytopenia should be undertaken in facilities with appropriate expertise in ultrasound imaging and invasive fetal interventions, and that have access to specific blood products and neonatal intensive care. | ✓ | | | | | | | |
| **EOP24** | Pregnancies at risk of fetal anaemia should be assessed by Doppler ultrasound of the fetal middle cerebral artery peak systolic velocity, to determine whether fetal blood sampling and intrauterine transfusion are necessary. | ✓ | | | | | | | |

| RBC transfusion – indications, Hb thresholds and volume<br>*RBC transfusion in chronic anaemia* | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **R2**<br>**GRADE A** | In children and adolescents with sickle cell disease who have been assessed to be at increased risk of stroke,[a] a program of prophylactic RBC transfusions should be used in order to reduce stroke occurrence.[b]<br>[a] Assessed by transcranial Doppler ultrasonography[10] and MRI.[11]<br>[b] See PP11 for methods of assessment. | | | | | | | ✓ | |
| **PP11** | Children and adolescents with sickle cell disease should be assessed for stroke risk using both transcranial Doppler ultrasonography[10] and MRI.[11] | | | | | | | ✓ | |
| **R4**<br>**GRADE B** | In paediatric patients with sickle cell disease, hydroxyurea should not be given for the primary purpose of reducing transfusion incidence.[a, b]<br>[a] Although hydroxyurea reduces transfusion incidence, it may not be the optimal treatment for prevention of stroke.<br>[b] See R2 and PP22. | | | | | | | ✓ | |
| **PP22** | In paediatric patients over 9 months of age with sickle cell disease, hydroxyurea should be offered to reduce vaso-occlusive pain crises and acute chest syndromes. | | | | | | | ✓ | |
| **PP7** | In paediatric patients with beta thalassaemia, the evidence does not support any change to the current practice of maintaining a pretransfusion Hb concentration of 90–100 g/L.[a]<br>[a] See PP23 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | | | | | | ✓ | |
| **PP10** | In paediatric patients over 20 kg who are chronically transfused (e.g. haemoglobinopathies or bone marrow failure syndromes) a single-unit approach may not be appropriate. Instead, calculation of the transfusion volume (mL) should be based on weight and desired Hb increment. | | | | | | | ✓ | |
| **EOP9** | In both male and female chronically transfused patients, RBC should be selected to match RhD, C/c, E/e and K antigen status. | | | | | | | ✓ | |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **Reducing the need for RBC transfusion**<br>*Placental transfusion* | | | | | | | | | |
| **PP32** | In preterm infants, deferring cord clamping for between 30 seconds and 3 minutes may reduce transfusion volume and incidence, and incidence of intraventricular haemorrhage. However, the effect of this practice on other outcomes (death, major morbidity and neurodevelopmental outcomes) is uncertain or unknown, particularly in extremely preterm infants (e.g. <28 weeks) and in those who require active resuscitation. | ✓ | ✓ | | | | | | |
| **PP33** | In term infants, deferring cord clamping for at least 1 minute is likely to reduce the risk of iron deficiency at 3–6 months. This intervention should be considered in infants who do not require active resuscitation, provided that access to phototherapy for jaundice is available.[a]<br>[a] See McDonald et al (2013).[12] | ✓ | ✓ | | | | | | |
| **Reducing the need for RBC transfusion**<br>*Oral and/or parenteral iron* | | | | | | | | | |
| **R5**<br>**GRADE C** | In surgical paediatric patients with or at risk of iron deficiency anaemia, preoperative iron therapy is recommended.[a]<br>[a] See R4 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] | | ✓ | ✓ | ✓ | | | | |
| **PP24** | In neonatal and paediatric surgical patients in whom substantial blood loss is anticipated, preoperative anaemia and iron deficiency[a] should be identified, evaluated and managed to minimise RBC transfusion.[b]<br>[a] Iron deficiency can be present with a normal Hb.<br>[b] See Appendix H (*Paediatric haemoglobin assessment and optimisation template*) of Module 6[1] (or Appendix C within this document) for further information on the optimal dosing strategy. | ✓ | ✓ | ✓ | ✓ | ✓ | | | |
| **PP25** | To implement PP24, patients should be evaluated as early as possible so that scheduling of surgery can be coordinated with optimisation of the patient's Hb and iron stores. | ✓ | ✓ | ✓ | ✓ | ✓ | | | |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **PP13** | Preterm and low birth weight infants should receive iron supplementation as necessary to achieve the recommended nutrient intake. However, routine supplementation in excess of the recommended nutrient intake, to reduce transfusion incidence, is not supported. | ✓ | ✓ | | | | | | |
| **PP14** | Infants and children should receive sufficient dietary iron to achieve the adequate intake or recommended daily intake. If the adequate intake or recommended daily intake cannot be met by dietary means, iron supplementation is advised. | | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ |
| **PP15** | Infants and children in populations at high risk[a] of iron deficiency should be screened for this condition.[b]<br>[a] See Domellof et al (2014)[13] and Pottie et al (2011).[14]<br>[b] See Section 3.6 of Module 6.[1] | | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ |
| **PP16** | Infants and children with iron deficiency should be treated with iron supplements and dietary modifications. | | ✓ | ✓ | ✓ | ✓ | ✓ | | ✓ |
| **PP27** | Critically ill paediatric patients should receive iron supplementation as necessary to achieve the recommended nutrient intake. | | | | | ✓ | | | |
| **EOP32** | From 6 months of age, all infants and children should receive iron-rich foods. | | ✓ | | | | | | |
| **EOP33** | Cow's milk should not be given to infants before 12 months of age; from 12 months of age, cow's milk intake should not exceed 500 mL per day. | | ✓ | | | | | | |
| **EOP34** | IV iron should be administered according to a protocol relevant to the specific product being used:[a]<br>▪ IV iron formulations have different iron concentrations, maximum doses, dilutions and rates of administration; they are not interchangeable with regard to dose, dilution and rates of administration<br>▪ IV iron formulations should only ever be administered in an appropriate health-care setting with medical personnel and resuscitation facilities on site.<br>[a] See Appendix I (*Intravenous iron*) of Module 6[1] (or Appendix D within this document) for further information. | | ✓ | ✓ | ✓ | ✓ | | | |

| Reducing the need for RBC transfusion<br>*Erythropoiesis stimulating agents (ESAs)* | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **R3**<br>**GRADE C** | In preterm infants with low birth weight (<2500 g), the *routine* use of ESAs is not advised. | ✓ | ✓ | | | | | | |
| **PP17** | In paediatric patients receiving chemotherapy, the *routine* use of ESAs is not advised.<br>The use of ESAs may reduce transfusion incidence; however, the studies are underpowered to determine their effect on mortality and thromboembolic events, which are increased in the adult population.[a]<br>[a] See R2 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | ✓ | | | | | | ✓ |
| **PP18** | In paediatric patients with chronic kidney disease, ESA therapy to achieve a low to intermediate Hb target may be used to avoid RBC transfusion, after consideration of risks and benefits for the individual patient.[a, b, c]<br>[a] See R4 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4]<br>[b] The KDIGO guidelines[15] recommend a Hb target of 110–120 g/L for paediatric patients and state that individualisation of ESA therapy is reasonable because some patients may have improvements in quality of life at higher Hb concentration.<br>[c] The NICE guidelines[16] recommend a Hb target of 100–120 g/L for children aged 2 years and older, and 95–115 g/L for children younger than 2 years of age (reflecting the lower normal range in that age group). | | ✓ | | | | ✓ | | |
| **PP19** | In adult patients with chronic kidney disease, ESA therapy to achieve a Hb target of >130 g/L is not recommended because of increased morbidity; therefore, it is sensible to apply this limit to paediatric patients.[a]<br>[a] See R6 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | ✓ | | | | ✓ | | |
| **PP20** | ESA use is less effective in patients with chronic kidney disease who have absolute or functional iron deficiency.[a]<br>[a] See PP13 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | ✓ | | | | ✓ | | |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **PP21** | Where ESAs are indicated for the treatment or prevention of anaemia in neonatal and paediatric patients, they should be combined with iron therapy. | ✓ | ✓ | | | | ✓ | | |
| **PP23** | In neonatal and paediatric surgical patients, an ESA should only be prescribed in consultation with a paediatric haematologist, and should be combined with iron therapy. | ✓ | ✓ | ✓ | ✓ | | | | ✓ |
| **PP26** | In critically ill paediatric patients with anaemia, ESAs should not be *routinely* used.[a]<br>[a] This point is based on the lack of effect of ESAs on mortality in critically ill adult patients. See R2 in *Patient Blood Management Guidelines: Module 4 – Critical Care*.[5] | | ✓ | | | ✓ | | | |
| **Reducing the need for RBC transfusion**<br>***Reducing the need for exchange transfusion*** | | | | | | | | | |
| **R7**<br>**GRADE B** | In neonates with haemolytic disease of the fetus and newborn, the use of IVIg is not recommended. | ✓ | | | | | | | |
| **PP34** | Neonates at risk of haemolytic disease of the fetus and newborn should be promptly assessed after birth. Those at high risk of severe jaundice should receive intensive phototherapy. | ✓ | | | | | | | |
| **EOP6** | In maternity patients with a fetus affected by haemolytic disease of the fetus and newborn who is at high risk of early fetal hydrops or death, a course of weekly IVIg should be considered. | ✓ | | | | | | | |
| **Reducing the need for RBC transfusion**<br>***Reducing blood loss*** | | | | | | | | | |
| **R8**<br>**GRADE B** | In paediatric patients undergoing surgery, measures to prevent hypothermia should be used.[a]<br>[a] See R12 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] | | | ✓ | ✓ | | | | |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **R9**<br>**GRADE C** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, the use of antifibrinolytics is suggested.[a, b, c]<br>[a] Although there is evidence of a reduction in transfusion, there is insufficient evidence to determine the risk of thromboembolic complications.<br>[b] Tranexamic acid in this context is approved in Australia. The use of aprotinin in this context is considered off label in Australia. Epsilon-aminocaproic acid is not licensed for use in Australia.<br>[c] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. | | | ✓ | | | | | |
| **R10**<br>**GRADE C** | In paediatric patients undergoing surgery for scoliosis in whom substantial blood loss is anticipated, the use of antifibrinolytics may be considered.[a, b]<br>[a] Tranexamic acid in this context is approved in Australia. The use of aprotinin in this context is considered off label in Australia. Epsilon-aminocaproic acid is not licensed for use in Australia.<br>[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. | | | | ✓ | | | | |
| **R11**<br>**GRADE C** | In paediatric patients undergoing craniofacial surgery in whom substantial blood loss is anticipated, the use of antifibrinolytics may be considered.[a, b]<br>[a] Tranexamic acid in this context is approved in Australia. The use of aprotinin in this context is considered off label in Australia. Epsilon-aminocaproic acid is not licensed for use in Australia.<br>[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. | | | | ✓ | | | | |
| **R12**<br>**GRADE C** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, the *routine* use of rFVIIa is not recommended. | | | ✓ | | | | | |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **PP40** | The administration of rFVIIa may be considered in the perioperative patient with life-threatening haemorrhage after conventional measures, including surgical haemostasis, use of antifibrinolytics and appropriate blood component therapy have failed.[a, b]<br>[a] rFVIIa is not licensed for this use; its use should only be considered in exceptional circumstances.<br>[b] See R22 and PP20 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] | | | ✓ | ✓ | ✓ | | | |
| **PP38** | In acutely bleeding critically ill paediatric trauma patients, tranexamic acid should be administered within 3 hours of injury.[a, b]<br>[a] See R3 in *Patient Blood Management Guidelines: Module 4 – Critical Care*.[5]<br>[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. | | | | ✓ | ✓ | | | |
| **PP39** | In paediatric trauma patients aged under 12 years, a tranexamic acid dose of 15 mg/kg (maximum 1000 mg) infused intravenously over 10 minutes, followed by 2 mg/kg/hour (maximum 125 mg/hour) until bleeding is controlled or for up to 8 hours is suggested.[a, b]<br>[a] See the template given in Appendix K (*Critical bleeding protocol*) of Module 6[1] (or Appendix F within this document), which is intended for local adaptation.<br>[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. | | | | ✓ | ✓ | | | |
| **PP35** | In paediatric patients, acute normovolaemic haemodilution has not been shown to reduce transfusion or improve clinical outcomes. However, if acute normovolaemic haemodilution is used, it requires a local procedural guideline that addresses patient selection, vascular access, volume of blood withdrawn, choice of replacement fluid, blood storage and handling, and timing of reinfusion. | | | | ✓ | | | | |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **PP36** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, intraoperative cell salvage may be considered. If intraoperative cell salvage is used, it requires a local procedural guideline that should include patient selection, use of equipment and reinfusion. All staff operating cell salvage devices should receive appropriate training, to ensure knowledge of the technique and proficiency in using it. | | | ✓ | | | | | |
| **PP37** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, viscoelastic point-of-care testing may be considered. | | | ✓ | | | | | |
| **EOP27** | Strategies to safely minimise phlebotomy losses should be used for all neonatal and paediatric patients. Such strategies may include (where safe and feasible):<br>▪ use of 'as-needed' rather than routine sampling<br>▪ meticulous avoidance of blood overdraw<br>▪ return of void volumes to sampling lines<br>▪ use of closed inline sampling devices<br>▪ judicious use and 'on-time' removal of sampling lines<br>▪ optimal sampling technique and sample handling to minimise rejection of samples by laboratory<br>▪ laboratory equipment that uses the smallest possible sample volumes<br>▪ use of non-invasive techniques and point-of-care devices<br>▪ audit compliance and cumulative phlebotomy losses in selected groups of patients at regular intervals. | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| **EOP28** | Prothrombin complex concentrates may be considered in neonatal and paediatric patients undergoing urgent surgery who are receiving vitamin K antagonists.[17] | ✓ | ✓ | ✓ | ✓ | ✓ | | | |
| **EOP29** | Prothrombin complex concentrates may be considered to treat bleeding in paediatric patients at high risk of volume overload (e.g. those who have undergone cardiac surgery on cardiopulmonary bypass). | | ✓ | ✓ | | | | | |
| **EOP30** | Topical haemostatic agents may be considered in neonatal and paediatric surgical patients as an adjuvant to control bleeding. | | ✓ | ✓ | ✓ | | | | |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **EOP31** | The use of topical haemostatic agents should adhere to the manufacturer's instructions and safety information. | | ✓ | ✓ | ✓ | | | | |
| **Measures to reduce coagulopathy**<br>*Platelets* | | | | | | | | | |
| **PP28** | In neonatal and paediatric patients, the decision to transfuse platelets should take into account the potential risks and benefits. The decision should be based not only on laboratory investigations but also on assessment of the patient's clinical condition. Factors that may influence the decision include active bleeding, medications affecting platelet function and coagulation status, and congenital and acquired bleeding disorders. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **PP31** | In patients undergoing chemotherapy and haematopoietic stem cell transplantation, the recommended strategy for prophylactic use of platelets is transfusion at a platelet count of $<10 \times 10^9$/L in the absence of risk factors, and at $<20 \times 10^9$/L in the presence of risk factors (e.g. fever, minor bleeding).[a]<br>[a] See R8 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | | | | | | | ✓ |
| **EOP4** | In general, neonatal and paediatric patients with a platelet count $\geq 50 \times 10^9$/L can undergo invasive procedures without any serious bleeding; however, lower platelet counts may be tolerated.[a]<br>[a] See PP17 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **EOP25** | Pregnant women who have had a prior pregnancy with fetal or neonatal intracranial haemorrhage or thrombocytopenia due to fetal and neonatal alloimmune thrombocytopenia should be managed with IVIg.[18] | ✓ | | | | | | | |
| **EOP26** | Fetal blood sampling should be considered to assess response to IVIg in those who have had a previous child with intracranial haemorrhage due to fetal and neonatal alloimmune thrombocytopenia. The risk of fetal blood sampling should be balanced against the risk of bleeding due to suboptimal IVIg response. | ✓ | | | | | | | |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **EOP16** | For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia:<br>▪ urgent platelet transfusion should be given if platelets are below $30 \times 10^9$/L in a term infant or below $50 \times 10^9$/L in a preterm infant, even in the absence of clinically significant bleeding<br>▪ if there is active bleeding, a higher threshold should be considered ($100 \times 10^9$/L for intracranial bleeding, and $50 \times 10^9$/L for other sites of bleeding)<br>▪ in all cases, a paediatric haematologist should be consulted. | ✓ | | | | | | | |
| **EOP17** | For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia, platelet count response to transfusion should be checked within 12 hours. | ✓ | | | | | | | |
| **EOP18** | For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia, random donor platelets should be used if antigen-matched platelets are not immediately available. Continued use of random donor platelets is acceptable if antigen-matched platelets cannot be obtained.<br>Because of short survival of random donor platelets, repeated transfusion is likely to be needed. | ✓ | | | | | | | |
| **EOP19** | For neonates with fetal and neonatal alloimmune thrombocytopenia, IVIg may be considered.[18] | ✓ | | | | | | | |
| **EOP20** | For neonatal and paediatric patients with platelet refractoriness attributable to non-immune causes such as splenomegaly or infection, fresh, ABO-compatible, single-donor apheresis platelets may improve platelet increment. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **EOP21** | If the cause of platelet refractoriness is not obvious, investigation should include screening for HLA antibodies. HLA-matched platelets should be used if an HLA antibody is detected.<br>If the HLA antibody screen is negative or there is a poor response to HLA-matched platelets, screening for human platelet antigen antibodies should be undertaken, followed by use of human platelet antigen-matched platelets if positive. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **EOP22** | In patients with inherited platelet disorders such as Bernard Soulier Syndrome and Glanzmann's thrombasthenia, platelet transfusions should be avoided if possible, to reduce the patient's risk of alloimmunisation. If platelet transfusion is unavoidable the patient should receive HLA-matched platelets. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **Measures to reduce coagulopathy**<br>***Fresh frozen plasma (FFP), cryoprecipitate or fibrinogen concentrate*** | | | | | | | | | |
| **R6**<br>**GRADE C** | In neonatal and paediatric patients undergoing cardiac surgery, the *routine* use of an FFP-based pump prime solution is not recommended, because it offers no advantages over an albumin-based solution in relation to postoperative blood loss, or perioperative transfusion requirements. | | | ✓ | | | | | |
| **PP29** | In neonatal and paediatric patients, the decision to transfuse FFP, cryoprecipitate or fibrinogen concentrate should take into account the potential risks and benefits. The decision should be based not only on laboratory investigations but also on assessment of the patient's clinical condition. Factors that may influence the decision include active bleeding, medications affecting coagulation status, and congenital and acquired bleeding disorders. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **PP30** | For guidance on the use of FFP in specific patient groups, refer to:[a]<br>▪ *Patient Blood Management Guidelines: Module 1 – Critical Bleeding/Massive Transfusion (2011)*[2]<br>▪ *Patient Blood Management Guidelines: Module 2 – Perioperative (2012)*[3]<br>▪ *Warfarin Reversal: Consensus Guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis (2004)*[19]<br>▪ AHCDO guidelines for patients with specific factor deficiencies (www.ahcdo.org.au)<br>▪ *Guidelines for the Use of Fresh-Frozen Plasma, Cryoprecipitate and Cryosupernatant (2004).*[20]<br>[a] See PP17 in *Patient Blood Management Guidelines: Module 3 – Medical.*[4] | ✓ | | ✓ | ✓ | ✓ | | | ✓ |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **EOP1** | In neonatal and paediatric patients undergoing surgery, FFP is only indicated for treatment of active bleeding where coagulopathy is a contributing factor. Its use should be guided by clinical assessment, supplemented by point-of-care or laboratory testing. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **EOP2** | In general, neonatal and paediatric patients with an INR ≤2 can undergo invasive procedures without any serious bleeding; however, higher INRs may be tolerated.[a]<br>[a] See PP17 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **EOP3** | Cryoprecipitate should be used to treat active bleeding when the fibrinogen level is <1.5 g/L. A target level of 2 g/L may be appropriate in certain situations (e.g. when critical bleeding is occurring or anticipated).[a]<br>[a] The template given in Appendix K (*Critical bleeding protocol*) of Module 6[1] (or Appendix F within this document) is intended for local adaptation. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **EOP5** | Specialist guidelines or haematology advice should be sought for at-risk patients undergoing intracranial, intraocular and neuraxial procedures, and for patients with severe thrombocytopenia or coagulopathy. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **Specific products for selected patients**<br>***Indications for 'fresh', irradiated or cytomegalovirus (CMV) negative blood products*** | | | | | | | | | |
| **EOP7** | 'Fresh' (<7 days) RBCs are not advocated for routine use, but may be considered in the following clinical situations:<br>▪ intrauterine transfusion (<5 days, if available)<br>▪ large-volume transfusion (>25 mL/kg)<br>▪ exchange transfusion<br>▪ cardiac surgery<br>▪ transfusion-dependent chronic anaemia (RBCs <14 days)<br>▪ where irradiated blood products are used. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **EOP10** | Irradiated cellular blood products (RBCs and platelets) are used to prevent transfusion-associated graft-versus-host disease, and are indicated for:<br>▪ intrauterine transfusion, and recipients of prior intrauterine transfusion up to 6 months of age<br>▪ suspected or known severe congenital T-cell immunodeficiency (e.g. severe combined immunodeficiency)<br>▪ severe acquired T-cell dysfunction, related to either disease or drug therapy (see published guidelines)[21-22]<br>▪ human leukocyte antigen-matched cellular blood products (RBCs, platelets and granulocytes). They may also be considered for:<br>▪ neonatal exchange transfusion, provided this does not unduly delay transfusion<br>▪ very low birth weight neonates, especially extremely preterm (<28 weeks) or extremely low birth weight infants<br>▪ certain patients undergoing chemotherapy (depending on degree of immunosuppression). | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **EOP11** | Stem cells must not be irradiated. | | | | | | | | ✓ |
| **EOP12** | Hyperkalaemia may occur when large volumes of irradiated blood are transfused. In patients at risk, irradiated blood should be as fresh as possible (<7 days) and used within 24 hours of irradiation. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **EOP13** | Patients at high risk of transfusion-associated graft-versus-host disease should be informed of the need for irradiated blood products. Also, alerts should be incorporated in the information systems of the health service and transfusion laboratory. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |

| | | Fetal and neonatal conditions | Preventing anaemia | Cardiac and cardiac surgical | Other surgical | Critically ill infant and child | Chronic kidney disease | Other chronic anaemia | Cancer, chemotherapy and transplantation |
|---|---|---|---|---|---|---|---|---|---|
| **EOP14** | CMV-negative products may be considered in the following situations:<br>▪ intrauterine transfusion<br>▪ preterm neonates (up to 28 days after expected date of delivery)<br>▪ patients with severe combined immunodeficiency who are CMV negative<br>▪ stem cell transplantation where both donor and recipient are known to be CMV negative<br>▪ granulocyte transfusions for recipients who are CMV seronegative, or whose status is unknown.<br>CMV-negative products are generally not required in other clinical settings. | ✓ | | | | ✓ | | | ✓ |
| **EOP15** | In urgent situations, if CMV-seronegative blood components are not available, CMV-unscreened leucodepleted components should be used to avoid delays. | ✓ | | | ✓ | | | | ✓ |
| Critical bleeding<br>*Bedside and laboratory response to critical bleeding* | | | | | | | | | |
| **EOP35** | Institutions that provide care for neonates and paediatric patients should have a critical bleeding protocol specific to such patients. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **EOP36** | The critical bleeding protocol should outline the essential steps (including coordination and communication) to rapidly and effectively manage a patient who is at risk of or undergoing critical bleeding. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |
| **EOP37** | The critical bleeding protocol should include weight adjustments to guide blood product supply and administration. The clinician, in consultation with the haematologist or transfusion specialist, should tailor the type, volume and order of products given to the clinical circumstances. | ✓ | | ✓ | ✓ | ✓ | | | ✓ |

AHCDO, Australian Haemophilia Centre Directors' Organisation; CRG, Clinical/Consumer Reference Group; EOP, expert opinion point; ESA, erythropoiesis stimulating agent; FFP, fresh frozen plasma; HLA, human leucocyte antigen; IV, intravenous; IVIg, intravenous immunoglobulin; K, Kell; KDIGO, Kidney Disease Improving Global Outcomes; MRI, magnetic resonance imaging; NICE, National Institute for Health and Care Excellence; PP, practice point; R, recommendation; RBC, red blood cell

# 6. Recommendations, practice points and expert opinion points with links to age group

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **Red blood cell (RBC) transfusion – indications, Hb thresholds and volume** *RBC transfusion* | | | | | | |
| **R1** **GRADE C** | In paediatric patients, including those who are critically ill, a restrictive transfusion strategy is suggested.[a, b, c]<br>[a] See PP6 for guidance on a restrictive transfusion strategy.<br>[b] Higher Hb thresholds may be appropriate in very low birth weight and preterm neonates.<br>[c] See PP2, PP3 and Appendix F *(RBC transfusions in preterm infants)* of Module 6[1] (or Appendix A within this document) for guidance for preterm neonates. | | | ✓ | ✓ | ✓ |
| **PP1** | In neonatal and paediatric patients, the decision to give a RBC transfusion should not be dictated by a Hb concentration alone.[a] The decision should also be based on assessment of the patient's underlying condition, anaemia-related signs and symptoms, and response to previous transfusions. Underlying conditions that may influence the decision to transfuse include acquired or congenital cardiac disease, and severe respiratory disease.<br>[a] See PP1 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | ✓ | ✓ | ✓ | ✓ |
| **PP6** | In haemodynamically stable paediatric patients (excluding neonates), evidence from other patient groups and CRG consensus[a] suggests that, with a:<br>▪ Hb concentration <70 g/L, RBC transfusion is often appropriate. However, transfusion may not be required in well-compensated patients or where other specific therapy is available.<br>▪ Hb concentration of 70–90 g/L, RBC transfusion may be appropriate. The decision to transfuse patients should be based on the need to relieve clinical signs and symptoms of anaemia, and the patient's response to previous transfusions.<br>▪ Hb concentration >90 g/L, RBC transfusion is often unnecessary and may be inappropriate.<br>[a] See PP3 in *Patient Blood Management Guidelines: Module 4 – Critical Care*.[5] | | | | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **PP5** | For neonatal and paediatric patients, a specific procedural guideline for RBC transfusion should be used that includes the following:<br>▪ age-specific Hb reference ranges<br>▪ volume of transfusion and rate of administration<br>▪ patient monitoring during and after transfusion<br>▪ transfusion technique (e.g. use of syringe pumps)<br>▪ recognition and reporting of adverse events. | | ✓ | ✓ | ✓ | ✓ |
| **PP8** | In paediatric patients less than 20 kg, calculate transfusion volume (mL) based on weight and desired Hb increment.[a, b]<br>[a] See Appendix F (*RBC transfusions in preterm infants)* of Module 6[1] (or Appendix A within this document).<br>[b] See Appendix G *(Transfusion volume calculation for neonates, infants and small children)* of Module 6[1] (or Appendix B within this document). | | | | ✓ | |
| **PP9** | In most paediatric patients over 20 kg, transfusion of a single unit of RBC, followed by clinical reassessment to determine the need for further transfusion, is appropriate. This reassessment will also guide the decision on whether to retest the Hb level.[a]<br>[a] See PP2 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] | | | | | ✓ |
| **PP3** | In preterm infants requiring transfusion, there is insufficient evidence to support or refute the use of either a restrictive or liberal RBC transfusion strategy. | | ✓ | | | |
| **PP2** | Neonatal units should use a procedural guideline[a] for RBC transfusion in preterm infants that includes the following:<br>▪ age of infant<br>▪ age-specific Hb reference ranges<br>▪ Hb or haematocrit<br>▪ level of respiratory support<br>▪ ongoing or anticipated red cell loss<br>▪ nutritional status.<br>[a] See Appendix F (*RBC transfusions in preterm infants)* of Module 6[1] (or Appendix A within this document). | | ✓ | ✓ | | |
| **PP4** | In neonatal patients, calculate transfusion volume (mL) based on weight and desired Hb increment.[a, b]<br>[a] See Appendix F (*RBC transfusions in preterm infants*) of Module 6[1] (or Appendix A within this document).<br>[b] See Appendix G *(Transfusion volume calculation for neonates, infants and small children)* of Module 6[1] (or Appendix B within this document). | | ✓ | ✓ | | |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **PP12** | In neonatal and paediatric patients with critical bleeding requiring massive transfusion, use a critical bleeding protocol.[a] A template protocol is provided within the module.[b]<br>[a] The use of the word 'protocol' is not strictly prescriptive.<br>[b] The template given in Appendix K (*Critical bleeding protocol*) of Module 6[1] (or Appendix F within this document) is intended for local adaptation. | | ✓ | ✓ | ✓ | ✓ |
| **EOP8** | Where possible, K-negative RBC should be selected for transfusion for all females of childbearing potential who are K negative or whose K antigen status is unable to be determined prior to transfusion. This includes fetal transfusion. | ✓ | ✓ | ✓ | ✓ | ✓ |
| **EOP23** | Management of pregnancies at risk of fetal anaemia or thrombocytopenia should be undertaken in facilities with appropriate expertise in ultrasound imaging and invasive fetal interventions, and that have access to specific blood products and neonatal intensive care. | ✓ | | | | |
| **EOP24** | Pregnancies at risk of fetal anaemia should be assessed by Doppler ultrasound of the fetal middle cerebral artery peak systolic velocity, to determine whether fetal blood sampling and intrauterine transfusion are necessary. | ✓ | | | | |
| **RBC transfusion – indications, Hb thresholds and volume**<br>***RBC transfusion in chronic anaemia*** | | | | | | |
| **R2**<br>**GRADE A** | In children and adolescents with sickle cell disease who have been assessed to be at increased risk of stroke,[a] a program of prophylactic RBC transfusions should be used in order to reduce stroke occurrence.[b]<br>[a] Assessed by transcranial Doppler ultrasonography[10] and MRI.[11]<br>[b] See PP11 for methods of assessment. | | | | ✓ | ✓ |
| **PP11** | Children and adolescents with sickle cell disease should be assessed for stroke risk using both transcranial Doppler ultrasonography[10] and MRI.[11] | | | | ✓ | ✓ |
| **R4**<br>**GRADE B** | In paediatric patients with sickle cell disease, hydroxyurea should not be given for the primary purpose of reducing transfusion incidence.[a, b]<br>[a] Although hydroxyurea reduces transfusion incidence, it may not be the optimal treatment for prevention of stroke.<br>[b] See R2 and PP22. | | | | ✓ | ✓ |
| **PP22** | In paediatric patients over 9 months of age with sickle cell disease, hydroxyurea should be offered to reduce vaso-occlusive pain crises and acute chest syndromes. | | | | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **PP7** | In paediatric patients with beta thalassaemia, the evidence does not support any change to the current practice of maintaining a pretransfusion Hb concentration of 90–100 g/L.[a]<br>[a] See PP23 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | | | ✓ | ✓ |
| **PP10** | In paediatric patients over 20 kg who are chronically transfused (e.g. haemoglobinopathies or bone marrow failure syndromes) a single-unit approach may not be appropriate. Instead, calculation of the transfusion volume (mL) should be based on weight and desired Hb increment. | | | | | ✓ |
| **EOP9** | In both male and female chronically transfused patients, RBC should be selected to match RhD, C/c, E/e and K antigen status. | | | | ✓ | ✓ |
| **Reducing the need for RBC transfusion**<br>***Placental transfusion*** | | | | | | |
| **PP32** | In preterm infants, deferring cord clamping for between 30 seconds and 3 minutes may reduce transfusion volume and incidence, and incidence of intraventricular haemorrhage. However, the effect of this practice on other outcomes (death, major morbidity and neurodevelopmental outcomes) is uncertain or unknown, particularly in extremely preterm infants (e.g. <28 weeks) and in those who require active resuscitation. | | ✓ | | | |
| **PP33** | In term infants, deferring cord clamping for at least 1 minute is likely to reduce the risk of iron deficiency at 3–6 months. This intervention should be considered in infants who do not require active resuscitation, provided that access to phototherapy for jaundice is available.[a]<br>[a] See McDonald et al (2013).[12] | | | ✓ | | |
| **Reducing the need for RBC transfusion**<br>***Oral and/or parenteral iron*** | | | | | | |
| **R5**<br>**GRADE C** | In surgical paediatric patients with or at risk of iron deficiency anaemia, preoperative iron therapy is recommended.[a]<br>[a] See R4 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] | | ✓ | ✓ | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **PP24** | In neonatal and paediatric surgical patients in whom substantial blood loss is anticipated, preoperative anaemia and iron deficiency[a] should be identified, evaluated and managed to minimise RBC transfusion.[b]<br>[a] Iron deficiency can be present with a normal Hb.<br>[b] See Appendix H (*Paediatric haemoglobin assessment and optimisation template*) of Module 6[1] (or Appendix C within this document) for further information on the optimal dosing strategy. | | ✓ | ✓ | ✓ | ✓ |
| **PP25** | To implement PP24, patients should be evaluated as early as possible so that scheduling of surgery can be coordinated with optimisation of the patient's Hb and iron stores. | | ✓ | ✓ | ✓ | ✓ |
| **PP13** | Preterm and low birth weight infants should receive iron supplementation as necessary to achieve the recommended nutrient intake. However, routine supplementation in excess of the recommended nutrient intake, to reduce transfusion incidence, is not supported. | | ✓ | ✓ | | |
| **PP14** | Infants and children should receive sufficient dietary iron to achieve the adequate intake or recommended daily intake. If the adequate intake or recommended daily intake cannot be met by dietary means, iron supplementation is advised. | | | ✓ | ✓ | ✓ |
| **PP15** | Infants and children in populations at high risk[a] of iron deficiency should be screened for this condition.[b]<br>[a] See Domellof et al (2014)[13] and Pottie et al (2011).[14]<br>[b] See Section 3.6 of Module 6.[1] | | | | ✓ | ✓ |
| **PP16** | Infants and children with iron deficiency should be treated with iron supplements and dietary modifications. | | | | ✓ | ✓ |
| **PP27** | Critically ill paediatric patients should receive iron supplementation as necessary to achieve the recommended nutrient intake. | | | | ✓ | ✓ |
| **EOP32** | From 6 months of age, all infants and children should receive iron-rich foods. | | | | ✓ | ✓ |
| **EOP33** | Cow's milk should not be given to infants before 12 months of age; from 12 months of age, cow's milk intake should not exceed 500 mL per day. | | ✓ | ✓ | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **EOP34** | IV iron should be administered according to a protocol relevant to the specific product being used: [a]<br>▪ IV iron formulations have different iron concentrations, maximum doses, dilutions and rates of administration; they are not interchangeable with regard to dose, dilution and rates of administration<br>▪ IV iron formulations should only ever be administered in an appropriate health-care setting with medical personnel and resuscitation facilities on site.<br>[a] See Appendix I (*Intravenous iron*) of Module 6[1] (or Appendix D within this document) for further information. | | ✓ | ✓ | ✓ | ✓ |
| **Reducing the need for RBC transfusion**<br>***Erythropoiesis stimulating agents (ESAs)*** | | | | | | |
| **R3**<br>**GRADE C** | In preterm infants with low birth weight (<2500 g), the *routine* use of ESAs is not advised. | | ✓ | ✓ | | |
| **PP17** | In paediatric patients receiving chemotherapy, the *routine* use of ESAs is not advised.<br>The use of ESAs may reduce transfusion incidence; however, the studies are underpowered to determine their effect on mortality and thromboembolic events, which are increased in the adult population.[a]<br>[a] See R2 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | | | ✓ | ✓ |
| **PP18** | In paediatric patients with chronic kidney disease, ESA therapy to achieve a low to intermediate Hb target may be used to avoid RBC transfusion, after consideration of risks and benefits for the individual patient.[a, b, c]<br>[a] See R4 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4]<br>[b] The KDIGO guidelines[15] recommend a Hb target of 110–120 g/L for paediatric patients and state that individualisation of ESA therapy is reasonable because some patients may have improvements in quality of life at higher Hb concentration.<br>[c] The NICE guidelines[16] recommend a Hb target of 100–120 g/L for children aged 2 years and older, and 95–115 g/L for children younger than 2 years of age (reflecting the lower normal range in that age group). | | | | ✓ | ✓ |
| **PP19** | In adult patients with chronic kidney disease, ESA therapy to achieve a Hb target of >130 g/L is not recommended because of increased morbidity; therefore, it is sensible to apply this limit to paediatric patients.[a]<br>[a] See R6 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | | | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **PP20** | ESA use is less effective in patients with chronic kidney disease who have absolute or functional iron deficiency.[a]<br>[a] See PP13 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | | | ✓ | ✓ |
| **PP21** | Where ESAs are indicated for the treatment or prevention of anaemia in neonatal and paediatric patients, they should be combined with iron therapy. | | ✓ | ✓ | ✓ | ✓ |
| **PP23** | In neonatal and paediatric surgical patients, an ESA should only be prescribed in consultation with a paediatric haematologist, and should be combined with iron therapy. | | ✓ | ✓ | ✓ | ✓ |
| **PP26** | In critically ill paediatric patients with anaemia, ESAs should not be *routinely* used.[a]<br>[a] This point is based on the lack of effect of ESAs on mortality in critically ill adult patients. See R2 in *Patient Blood Management Guidelines: Module 4 – Critical Care*.[5] | | | | ✓ | ✓ |
| **Reducing the need for RBC transfusion**<br>***Reducing the need for exchange transfusion*** | | | | | | |
| **R7**<br>**GRADE B** | In neonates with haemolytic disease of the fetus and newborn, the use of IVIg is not recommended. | | ✓ | ✓ | | |
| **PP34** | Neonates at risk of haemolytic disease of the fetus and newborn should be promptly assessed after birth. Those at high risk of severe jaundice should receive intensive phototherapy. | | ✓ | ✓ | | |
| **EOP6** | In maternity patients with a fetus affected by haemolytic disease of the fetus and newborn who is at high risk of early fetal hydrops or death, a course of weekly IVIg should be considered. | ✓ | | | | |
| **Reducing the need for RBC transfusion**<br>***Reducing blood loss*** | | | | | | |
| **R8**<br>**GRADE B** | In paediatric patients undergoing surgery, measures to prevent hypothermia should be used.[a]<br>[a] See R12 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] | | ✓ | ✓ | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **R9** **GRADE C** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, the use of antifibrinolytics is suggested.[a, b, c]<br>[a] Although there is evidence of a reduction in transfusion, there is insufficient evidence to determine the risk of thromboembolic complications.<br>[b] Tranexamic acid in this context is approved in Australia. The use of aprotinin in this context is considered off label in Australia. Epsilon-aminocaproic acid is not licensed for use in Australia.<br>[c] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. | | | ✓ | ✓ | ✓ |
| **R10** **GRADE C** | In paediatric patients undergoing surgery for scoliosis in whom substantial blood loss is anticipated, the use of antifibrinolytics may be considered.[a, b]<br>[a] Tranexamic acid in this context is approved in Australia. The use of aprotinin in this context is considered off label in Australia. Epsilon-aminocaproic acid is not licensed for use in Australia.<br>[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. | | | | | ✓ |
| **R11** **GRADE C** | In paediatric patients undergoing craniofacial surgery in whom substantial blood loss is anticipated, the use of antifibrinolytics may be considered.[a, b]<br>[a] Tranexamic acid in this context is approved in Australia. The use of aprotinin in this context is considered off label in Australia. Epsilon-aminocaproic acid is not licensed for use in Australia.<br>[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. | | | | ✓ | ✓ |
| **R12** **GRADE C** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, the *routine* use of rFVIIa is not recommended. | | | ✓ | ✓ | ✓ |
| **PP40** | The administration of rFVIIa may be considered in the perioperative patient with life-threatening haemorrhage after conventional measures, including surgical haemostasis, use of antifibrinolytics and appropriate blood component therapy have failed.[a, b]<br>[a] rFVIIa is not licensed for this use; its use should only be considered in exceptional circumstances.<br>[b] See R22 and PP20 in *Patient Blood Management Guidelines: Module 2 – Perioperative.*[3] | | | ✓ | ✓ | ✓ |
| **PP38** | In acutely bleeding critically ill paediatric trauma patients, tranexamic acid should be administered within 3 hours of injury.[a, b]<br>[a] See R3 in *Patient Blood Management Guidelines: Module 4 – Critical Care.*[5]<br>[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. | | | | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **PP39** | In paediatric trauma patients aged under 12 years, a tranexamic acid dose of 15 mg/kg (maximum 1000 mg) infused intravenously over 10 minutes, followed by 2 mg/kg/hour (maximum 125 mg/hour) until bleeding is controlled or for up to 8 hours is suggested.[a, b]<br>[a] See the template given in Appendix K (*Critical bleeding protocol*) of Module 6[1] (or Appendix F within this document), which is intended for local adaptation.<br>[b] See Appendix J (*Tranexamic acid dosing guidance*) of Module 6[1] (or Appendix E within this document) for further information. | | | | ✓ | ✓ |
| **PP35** | In paediatric patients, acute normovolaemic haemodilution has not been shown to reduce transfusion or improve clinical outcomes. However, if acute normovolaemic haemodilution is used, it requires a local procedural guideline that addresses patient selection, vascular access, volume of blood withdrawn, choice of replacement fluid, blood storage and handling, and timing of reinfusion. | | | | ✓ | ✓ |
| **PP36** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, intraoperative cell salvage may be considered. If intraoperative cell salvage is used, it requires a local procedural guideline that should include patient selection, use of equipment and reinfusion. All staff operating cell salvage devices should receive appropriate training, to ensure knowledge of the technique and proficiency in using it. | | | | ✓ | ✓ |
| **PP37** | In paediatric patients undergoing cardiac surgery with cardiopulmonary bypass, viscoelastic point-of-care testing may be considered. | | | ✓ | ✓ | ✓ |
| **EOP27** | Strategies to safely minimise phlebotomy losses should be used for all neonatal and paediatric patients. Such strategies may include (where safe and feasible):<br>▪ use of 'as-needed' rather than routine sampling<br>▪ meticulous avoidance of blood overdraw<br>▪ return of void volumes to sampling lines<br>▪ use of closed inline sampling devices<br>▪ judicious use and 'on-time' removal of sampling lines<br>▪ optimal sampling technique and sample handling to minimise rejection of samples by laboratory<br>▪ laboratory equipment that uses the smallest possible sample volumes<br>▪ use of non-invasive techniques and point-of-care devices<br>▪ audit compliance and cumulative phlebotomy losses in selected groups of patients at regular intervals. | | ✓ | ✓ | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **EOP28** | Prothrombin complex concentrates may be considered in neonatal and paediatric patients undergoing urgent surgery who are receiving vitamin K antagonists.[17] | | | ✓ | ✓ | ✓ |
| **EOP29** | Prothrombin complex concentrates may be considered to treat bleeding in paediatric patients at high risk of volume overload (e.g. those who have undergone cardiac surgery on cardiopulmonary bypass). | | | ✓ | ✓ | ✓ |
| **EOP30** | Topical haemostatic agents may be considered in neonatal and paediatric surgical patients as an adjuvant to control bleeding. | | ✓ | ✓ | ✓ | ✓ |
| **EOP31** | The use of topical haemostatic agents should adhere to the manufacturer's instructions and safety information. | | ✓ | ✓ | ✓ | ✓ |
| Measures to reduce coagulopathy<br>*Platelets* | | | | | | |
| **PP28** | In neonatal and paediatric patients, the decision to transfuse platelets should take into account the potential risks and benefits. The decision should be based not only on laboratory investigations but also on assessment of the patient's clinical condition. Factors that may influence the decision include active bleeding, medications affecting platelet function and coagulation status, and congenital and acquired bleeding disorders. | | ✓ | ✓ | ✓ | ✓ |
| **PP31** | In patients undergoing chemotherapy and haematopoietic stem cell transplantation, the recommended strategy for prophylactic use of platelets is transfusion at a platelet count of $<10 \times 10^9$/L in the absence of risk factors, and at $<20 \times 10^9$/L in the presence of risk factors (e.g. fever, minor bleeding).[a]<br>[a] See R8 in *Patient Blood Management Guidelines: Module 3 – Medical*.[4] | | | | ✓ | ✓ |
| **EOP4** | In general, neonatal and paediatric patients with a platelet count $\geq 50 \times 10^9$/L can undergo invasive procedures without any serious bleeding; however, lower platelet counts may be tolerated.[a]<br>[a] See PP17 in *Patient Blood Management Guidelines: Module 2 – Perioperative*.[3] | | ✓ | ✓ | ✓ | ✓ |
| **EOP25** | Pregnant women who have had a prior pregnancy with fetal or neonatal intracranial haemorrhage or thrombocytopenia due to fetal and neonatal alloimmune thrombocytopenia should be managed with IVIg.[18] | ✓ | | | | |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **EOP26** | Fetal blood sampling should be considered to assess response to IVIg in those who have had a previous child with intracranial haemorrhage due to fetal and neonatal alloimmune thrombocytopenia. The risk of fetal blood sampling should be balanced against the risk of bleeding due to suboptimal IVIg response. | ✓ | | | | |
| **EOP16** | For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia:<br>▪ urgent platelet transfusion should be given if platelets are below $30 \times 10^9$/L in a term infant or below $50 \times 10^9$/L in a preterm infant, even in the absence of clinically significant bleeding<br>▪ if there is active bleeding, a higher threshold should be considered ($100 \times 10^9$/L for intracranial bleeding, and $50 \times 10^9$/L for other sites of bleeding)<br>▪ in all cases, a paediatric haematologist should be consulted. | | ✓ | ✓ | | |
| **EOP17** | For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia, platelet count response to transfusion should be checked within 12 hours. | | ✓ | ✓ | | |
| **EOP18** | For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia, random donor platelets should be used if antigen-matched platelets are not immediately available. Continued use of random donor platelets is acceptable if antigen-matched platelets cannot be obtained. Because of short survival of random donor platelets, repeated transfusion is likely to be needed. | | ✓ | ✓ | | |
| **EOP19** | For neonates with fetal and neonatal alloimmune thrombocytopenia, IVIg may be considered.[18] | | ✓ | ✓ | | |
| **EOP20** | For neonatal and paediatric patients with platelet refractoriness attributable to non-immune causes such as splenomegaly or infection, fresh, ABO-compatible, single-donor apheresis platelets may improve platelet increment. | | ✓ | ✓ | ✓ | ✓ |
| **EOP21** | If the cause of platelet refractoriness is not obvious, investigation should include screening for HLA antibodies. HLA-matched platelets should be used if an HLA antibody is detected.<br>If the HLA antibody screen is negative or there is a poor response to HLA-matched platelets, screening for human platelet antigen antibodies should be undertaken, followed by use of human platelet antigen-matched platelets if positive. | | ✓ | ✓ | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **EOP22** | In patients with inherited platelet disorders such as Bernard Soulier Syndrome and Glanzmann's thrombasthenia, platelet transfusions should be avoided if possible, to reduce the patient's risk of alloimmunisation. If platelet transfusion is unavoidable the patient should receive HLA-matched platelets. | | ✓ | ✓ | ✓ | ✓ |
| **Measures to reduce coagulopathy**<br>***Fresh frozen plasma (FFP), cryoprecipitate or fibrinogen concentrate*** | | | | | | |
| **R6**<br>**GRADE C** | In neonatal and paediatric patients undergoing cardiac surgery, the *routine* use of an FFP-based pump prime solution is not recommended, because it offers no advantages over an albumin-based solution in relation to postoperative blood loss, or perioperative transfusion requirements. | | | ✓ | ✓ | ✓ |
| **PP29** | In neonatal and paediatric patients, the decision to transfuse FFP, cryoprecipitate or fibrinogen concentrate should take into account the potential risks and benefits. The decision should be based not only on laboratory investigations but also on assessment of the patient's clinical condition. Factors that may influence the decision include active bleeding, medications affecting coagulation status, and congenital and acquired bleeding disorders. | | ✓ | ✓ | ✓ | ✓ |
| **PP30** | For guidance on the use of FFP in specific patient groups, refer to:[a]<br>▪ *Patient Blood Management Guidelines: Module 1 – Critical Bleeding/Massive Transfusion (2011)*[2]<br>▪ *Patient Blood Management Guidelines: Module 2 – Perioperative (2012)*[3]<br>▪ *Warfarin Reversal: Consensus Guidelines, on behalf of the Australasian Society of Thrombosis and Haemostasis (2004)*[19]<br>▪ AHCDO guidelines for patients with specific factor deficiencies (www.ahcdo.org.au)<br>▪ *Guidelines for the Use of Fresh-Frozen Plasma, Cryoprecipitate and Cryosupernatant (2004).*[20]<br>[a] See PP17 in *Patient Blood Management Guidelines: Module 3 – Medical.*[4] | | ✓ | ✓ | ✓ | ✓ |
| **EOP1** | In neonatal and paediatric patients undergoing surgery, FFP is only indicated for treatment of active bleeding where coagulopathy is a contributing factor. Its use should be guided by clinical assessment, supplemented by point-of-care or laboratory testing. | | ✓ | ✓ | ✓ | ✓ |
| **EOP2** | In general, neonatal and paediatric patients with an INR ≤2 can undergo invasive procedures without any serious bleeding; however, higher INRs may be tolerated.[a]<br>[a] See PP17 in *Patient Blood Management Guidelines: Module 2 – Perioperative.*[3] | | ✓ | ✓ | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **EOP3** | Cryoprecipitate should be used to treat active bleeding when the fibrinogen level is <1.5 g/L. A target level of 2 g/L may be appropriate in certain situations (e.g. when critical bleeding is occurring or anticipated).[a]<br>[a] The template given in Appendix K (*Critical bleeding protocol*) of Module 6[1] (or Appendix F within this document) is intended for local adaptation. | | ✓ | ✓ | ✓ | ✓ |
| **EOP5** | Specialist guidelines or haematology advice should be sought for at-risk patients undergoing intracranial, intraocular and neuraxial procedures, and for patients with severe thrombocytopenia or coagulopathy. | | ✓ | ✓ | ✓ | ✓ |
| **Specific products for selected patients**<br>***Indications for 'fresh', irradiated or cytomegalovirus (CMV) negative blood products*** | | | | | | |
| **EOP7** | 'Fresh' (<7 days) RBCs are not advocated for routine use, but may be considered in the following clinical situations:<br>▪ intrauterine transfusion (<5 days, if available)<br>▪ large-volume transfusion (>25 mL/kg)<br>▪ exchange transfusion<br>▪ cardiac surgery<br>▪ transfusion-dependent chronic anaemia (RBCs <14 days)<br>▪ where irradiated blood products are used. | ✓ | ✓ | ✓ | ✓ | ✓ |
| **EOP10** | Irradiated cellular blood products (RBCs and platelets) are used to prevent transfusion-associated graft-versus-host disease, and are indicated for:<br>▪ intrauterine transfusion, and recipients of prior intrauterine transfusion up to 6 months of age<br>▪ suspected or known severe congenital T-cell immunodeficiency (e.g. severe combined immunodeficiency)<br>▪ severe acquired T-cell dysfunction, related to either disease or drug therapy (see published guidelines)[21-22]<br>▪ human leukocyte antigen-matched cellular blood products (RBCs, platelets and granulocytes).<br>They may also be considered for:<br>▪ neonatal exchange transfusion, provided this does not unduly delay transfusion<br>▪ very low birth weight neonates, especially extremely preterm (<28 weeks) or extremely low birth weight infants<br>▪ certain patients undergoing chemotherapy (depending on degree of immunosuppression). | ✓ | ✓ | ✓ | ✓ | ✓ |
| **EOP11** | Stem cells must not be irradiated. | | ✓ | ✓ | ✓ | ✓ |

| | | Fetus | Preterm VLBW neonate | Other neonate | Infant | Child or adolescent |
|---|---|---|---|---|---|---|
| **EOP12** | Hyperkalaemia may occur when large volumes of irradiated blood are transfused. In patients at risk, irradiated blood should be as fresh as possible (<7 days) and used within 24 hours of irradiation. | ✓ | ✓ | ✓ | ✓ | ✓ |
| **EOP13** | Patients at high risk of transfusion-associated graft-versus-host disease should be informed of the need for irradiated blood products. Also, alerts should be incorporated in the information systems of the health service and transfusion laboratory. | ✓ | ✓ | ✓ | ✓ | ✓ |
| **EOP14** | CMV-negative products may be considered in the following situations:<br>▪ intrauterine transfusion<br>▪ preterm neonates (up to 28 days after expected date of delivery)<br>▪ patients with severe combined immunodeficiency who are CMV negative<br>▪ stem cell transplantation where both donor and recipient are known to be CMV negative<br>▪ granulocyte transfusions for recipients who are CMV seronegative, or whose status is unknown.<br>CMV-negative products are generally not required in other clinical settings. | ✓ | ✓ | ✓ | ✓ | ✓ |
| **EOP15** | In urgent situations, if CMV-seronegative blood components are not available, CMV-unscreened leucodepleted components should be used to avoid delays. | ✓ | ✓ | ✓ | ✓ | ✓ |
| Critical bleeding<br>*Bedside and laboratory response to critical bleeding* | | | | | | |
| **EOP35** | Institutions that provide care for neonates and paediatric patients should have a critical bleeding protocol specific to such patients. | | ✓ | ✓ | ✓ | ✓ |
| **EOP36** | The critical bleeding protocol should outline the essential steps (including coordination and communication) to rapidly and effectively manage a patient who is at risk of or undergoing critical bleeding. | | ✓ | ✓ | ✓ | ✓ |
| **EOP37** | The critical bleeding protocol should include weight adjustments to guide blood product supply and administration. The clinician, in consultation with the haematologist or transfusion specialist, should tailor the type, volume and order of products given to the clinical circumstances. | | ✓ | ✓ | ✓ | ✓ |

AHCDO, Australian Haemophilia Centre Directors' Organisation; CRG, Clinical/Consumer Reference Group; EOP, expert opinion point; ESA, erythropoiesis stimulating agent; FFP, fresh frozen plasma; HLA, human leucocyte antigen; INR, international normalised ratio; IV, intravenous; IVIg, intravenous immunoglobulin; K, Kell; KDIGO, Kidney Disease Improving Global Outcomes; MRI, magnetic resonance imaging; NICE, National Institute for Health and Care Excellence; PP, practice point; R, recommendation; RBC, red blood cell; VLBW, very low birth weight

# 7. Product information

For information on blood products available in Australia, see the website of the Australian Red Cross Blood Service (www.transfusion.com.au).

For information on blood products available in New Zealand, see the website of the New Zealand Blood Service (www.nzblood.co.nz).

# Appendix A RBC transfusions in preterm infants

This appendix provides clinical guidance from the Clinical/Consumer Reference Group (CRG) on haemoglobin (Hb) thresholds for transfusion of preterm infants.

In the absence of clear evidence from high-quality trials, there is wide variation in such thresholds in international practice, as demonstrated by a recent survey of 1018 neonatologists in 22 countries.[23] For infants of extremely low birth weight or <28 week gestation, most neonatologists favoured Hb thresholds for transfusion of 95–120 g/L for infants not receiving mechanical ventilation, then decreasing thresholds over subsequent weeks. They favoured higher thresholds for infants receiving increased respiratory support in the form of supplemental oxygen.

New information is expected from large randomised controlled trials that are currently underway. Meanwhile, the CRG suggests that the values given in Table A.1 represent a reasonable approach to transfusion thresholds for preterm infants.

**Table A.1 Haemoglobin threshold for preterm infants**

| POSTNATAL WEEK | Hb (g/L) | |
|---|---|---|
| | NO RESPIRATORY SUPPORT | RESPIRATORY SUPPORT (e.g. supplemental oxygen, high-flow nasal cannula, CPAP, positive-pressure ventilation) |
| 1 | 100–120 | 110–130 |
| 2 | 85–110 | 100–125 |
| ≥3 | 70–100 | 85–110 |

CPAP, continuous positive airway pressure; Hb, haemoglobin

The threshold for transfusion within these ranges may be influenced by the presence of symptoms and other factors such as:

- anticipated blood loss (e.g. haemolysis, phlebotomy or surgery)
- quality of nutrition
- severity of illness
- site of sampling – Hb measured on blood samples obtained from a large artery or from veins tends to be lower than that from free-flowing capillary samples.[24]

In general, the decision to transfuse should be based on laboratory measurement of Hb rather than on estimates obtained from blood gas analysers, except in cases of clinical urgency. For guidance in calculating volume to transfuse, see Appendix B.

# Appendix B Transfusion volume calculation for neonates, infants and small children

In calculating transfusion volume for neonates, infants and small children:

- the dose or transfusion volume of blood components for neonates, infants and children should be carefully calculated and prescribed in mL (not in 'units'), with a specified transfusion rate
- an administration rate of up to 6 mL/kg/hour (for a 20 mL/kg transfusion) or 5 mL/kg/hour (for a 15 mL/kg transfusion) will allow proper checking procedures and completion of the transfusion within the 4 hours that RBCs can be out of a blood refrigerator.

Transfusion volume can be calculated using the following formula:[25]

**Transfusion volume (mL) =**
**patient's weight × EBV × (desired Hb – patient's Hb) / Hb of donor unit**

where:

- weight is in kg
- the patient's estimated blood volume (EBV) is in mL/kg – this decreases with age, from 100–120 mL/kg in extremely preterm infants, to 80–85 mL/kg in term infants and about 70 mL/kg in older infants and children
- desired Hb and patient's Hb is in g/L
- haematocrit (Hct) can be substituted for Hb in the formula, provided it is used throughout; Hb can be estimated from Hct using the formula Hb = Hct × 1000/3.

### Table B.1 Hct values

| CELL TYPE | Hct ± SD [RANGE] |
|---|---|
| Paediatric RBCs leucocyte depleted | 0.63 ± 0.03 [0.5–0.7] |
| RBCs leucocyte depleted | 0.59 ± 0.03 [0.5–0.7] |

Hct, haematocrit; RBC, red blood cell; SD, standard deviation

Source: Australian Red Cross Blood Service data (1 July 2013 to 30 June 2014)[a]

[a] http://www.transfusion.com.au/blood_products/components/red_cells

## Neonates

In neonates typical transfusion dose is 10–20mL/kg (where the upper end of the range applies to severe anaemia, expected ongoing risk factors or concurrent bleeding).

### Table B.2 Approximate Hb increments that can be expected following transfusion in neonates

| | ESTIMATED Hb (g/L) AFTER TRANSFUSION | | |
|---|---|---|---|
| CURRENT Hb (g/L) | TRANSFUSION OF 10 mL/kg | TRANSFUSION OF 15 mL/kg | TRANSFUSION OF 20 mL/kg |
| **Very preterm neonate with estimated blood volume 100 mL/kg** | | | |
| 70 | 91 | 102 | 112 |
| 80 | 101 | 112 | 122 |
| 90 | 111 | 122 | 132 |
| **Term neonate with estimated blood volume 80 mL/kg** | | | |
| 70 | 96 | 109 | 123 |
| 80 | 106 | 119 | 133 |
| 90 | 116 | 129 | 143 |

Hb, haemoglobin

## Infants and children less than 20 kg beyond the neonatal period

In infants and children less than 20 kg beyond the neonatal period, blood volume and Hb of donor unit are usually estimated to be similar for all patients, rather than varying transfusion by transfusion. Therefore, the formula can be simplified to the following:

**Transfusion volume (mL) =**
**patient's weight (kg) × (desired Hb [g/L] – patient's Hb [g/L]) × transfusion factor (0.5)**

Based on the typical Hct for Australian RBCs (see above), and assuming EBV = 70 mL/kg the 'transfusion factor' of 0.5 is suggested. Studies have shown that when calculating the transfusion volume that a transfusion factor of 0.3 and 0.4 are insufficient to achieve the desired Hb increment, and that a factor of 0.4.8 or 0.5.02 is more appropriate.[26-27]

A transfusion of 10 mL/kg is often sufficient and will increase Hb by approximately 20 g/L.

# Appendix C Paediatric haemoglobin assessment and optimisation template

## ANAEMIA[a]

### Hb below reference range for age, sex and gestation

| Ferritin <20 mcg/L<br>Iron deficiency anaemia | Ferritin 20–50 mcg/L<br>Possible iron deficiency anaemia | Ferritin >50 mcg/L<br>Unlikely iron deficiency anaemia |
|---|---|---|
| Review clinical history and identify cause (see Table C.1)<br><br>Start treatment:<br>▪ oral iron 3–6 mg/kg/day<br><br>Address causes of dietary iron deficiency:<br>▪ increase dietary iron<br>▪ if <1 year of age, cease cow's milk and use an infant formula<br>▪ if 1–2 years of age, reduce cow's milk to <500 mL daily<br><br>Assess haematological response within 2–4 weeks<br><br>Continue treatment for 3 months after Hb recovery<br><br>If oral iron is ineffective or is not tolerated, consider other causes of anaemia (see Column 3) and use of IV iron | Review and address any causes of iron deficiency (see Table C.1 and Column 1)<br><br>Correlate with MCV/MCH and CRP<br><br>Consider therapeutic trial of iron:<br>▪ oral iron 3 mg/kg/day<br><br>Assess haematological response within 2–4 weeks<br><br>If anaemia persists, consider other causes (see Column 3) | Correlate with MCH/MCV and CRP<br>Ferritin may be elevated in the setting of inflammation. However, iron deficiency may still be present, particularly where TSAT <20%.<br><br>Consider alternative causes of anaemia:<br>▪ thalassaemia and other haemoglobinopathies<br>▪ anaemia of chronic disease<br>▪ haemolytic anaemia<br>▪ B12 deficiency<br>▪ folate deficiency<br>▪ other |

CRP, C reactive protein; Hb, haemoglobin; IV, intravascular; MCH, mean corpuscular haemoglobin; MCV, mean corpuscular volume; TSAT, transferrin saturation.
[a] This algorithm applies to all patients, including those undergoing procedures in which substantial blood loss is anticipated.
The reference ranges are based on criteria from the Royal College of Pathologists of Australasia,[28] and they may require local adaptation.

## Table C.1 Age-specific differential diagnoses in children with iron deficiency

| INFANTS | CHILDREN | ADOLESCENT |
|---|---|---|
| Inadequate dietary iron<br>▪ Late introduction of iron-rich solids<br>▪ Early introduction (i.e. <12 months) of cow's milk<br>▪ Vegetarian or vegan diet | Inadequate dietary iron<br>▪ Vegetarian or vegan diet | Inadequate dietary iron<br>▪ Vegetarian or vegan diet |
| Increased iron requirements<br>▪ Catch-up growth if premature or low birth weight[a]<br>▪ Rapid growth period | Increased iron requirements<br>▪ Rapid growth period | Increased iron requirements<br>▪ Rapid growth period<br>▪ Pregnancy<br>▪ Extreme athletes |
| Intestinal blood loss<br>▪ Cow's milk protein intolerance<br>▪ Meckel's diverticulum<br>▪ Inflammatory bowel disease<br>▪ Parasitic infection<br>Other chronic blood loss such as epistaxis, or renal or pulmonary blood loss | Intestinal blood loss<br>▪ Meckel's diverticulum<br>▪ Inflammatory bowel disease<br>▪ Parasitic infection[b]<br>Other chronic blood loss such as epistaxis, or renal or pulmonary blood loss | Intestinal blood loss<br>▪ Inflammatory bowel disease<br>▪ Parasitic infection<br>▪ Menorrhagia<br>Other chronic blood loss such as epistaxis, or renal or pulmonary blood loss |
| Reduced absorption<br>▪ Coeliac disease<br>▪ Inflammatory bowel disease<br>▪ Gastric or intestinal surgeries<br>▪ *Helicobacter pylori* infection | Reduced absorption<br>▪ Coeliac disease<br>▪ Inflammatory bowel disease<br>▪ Gastric or intestinal surgeries<br>▪ *Helicobacter pylori* infection | Reduced absorption<br>▪ Coeliac disease<br>▪ Inflammatory bowel disease<br>▪ Gastric or intestinal surgeries<br>▪ *Helicobacter pylori* infection<br>▪ Dietary factor (tannins) |

[a] Antenatal risk factors that predispose an infant to iron deficiency include maternal iron deficiency, maternal diabetes mellitus, smoking and multiple pregnancies. Perinatal factors that predispose an infant to iron deficiency include low birth weight, prematurity, feto-maternal haemorrhage, twin-to-twin transfusion or other blood loss including placental abruption, subgaleal haemorrhage or iatrogenic blood loss.

[b] Giardia and hookworm infection

# Appendix D Intravenous iron

## D1 Introduction

### D1.1 Purpose

To ensure safe and appropriate administration of intravenous (IV) iron polymaltose, iron sucrose and iron carboxymaltose. Note that this guidance is based on practice guidelines from the Royal Children's Hospital, Mebourne.[29-30, 32]

### D1.2 Procedure

- Check for previous adverse reactions to IV iron before commencing infusion.
- Refer to package insert to ensure familiarity with adverse event profile for the specific product.
- Ensure that child and parent understand procedure:
  - obtain verbal consent to procedure
  - ensure that child and parent are aware of possible adverse reactions.
- Ensure that medication and treatment orders are correctly written up by the medical officer.
- Ensure that oxygen and resuscitation equipment are in working order.
- Ensure that there is an order for PRN adrenaline 0.01 mg/kg intramuscular (IM) 1:1000 in the event of anaphylaxis.
- Establish patient IV access and ensure that the IV is working well.
- Take blood specimens as requested.
- Commence infusion and observations as per protocol.
- Monitor for any local or systemic adverse reactions.
- If there are signs of an adverse reaction or anaphylaxis, cease the infusion immediately.
- Contact the treating medical officer or call the medical emergency team (MET).
- Treat symptomatically, and administer oxygen, IV fluids and adrenaline as required.

### D1.3 Precautions

- Ensure that all staff are familiar with MET criteria and can recognise when to initiate a MET call.
- Do not administer iron infusions out of hours unless they are urgently required and staffing levels are appropriate.
- Place the patient in a clinical area where the patient can be closely monitored throughout the duration of the infusion.
- Ensure that patients undergoing iron infusions are not on oral iron therapy, and that they do not recommence oral iron therapy until 1 week after the last dose of parenteral therapy.
- For iron sucrose and iron polymaltose:
  - consider premedications:
    - ceterizine (0.125 mg/kg oral; maximum 10 mg)
    - hydrocortisone (2–4 mg/kg IV; maximum 100 mg)
  - be aware that concomitant therapy with an angiotensin-converting enzyme (ACE) inhibitor may increase the incidence of adverse effects.

### D1.4 Contraindications

- Previous allergic reactions to iron therapy.
- Severe liver dysfunction.
- Iron overload.

### D1.5 Observations

- Baseline weight.
- Baseline temperature, respiratory rate, pulse and blood pressure.
- Direct observation for the first 15 minutes.
- For the remainder of the infusion, observe:
  - blood pressure every 15 minutes
  - heart rate for 60 minutes then hourly.
- Monitor for signs of anaphylaxis, headache, nausea, hypotension, joint and muscle pain or signs of extravasation.

### D1.6 Discharge

- Ensure patient meets discharge criteria.

**ALERT**

- Check prescription and vials carefully as there are many different forms of IV iron preparations.
- Iron formulations have different iron concentrations, maximum doses, dilutions and rates of administration and are not interchangeable with regard to dose, dilution and rates of administration.

## D2 Iron carboxymaltose (Ferinject) dose[29]

### Presentation

Two ampoule sizes:

- 100 mg/2 mL
- 500 mg/10 mL.

### Maximum dose

- Total or cumulative dose – may need to be administered over several doses at weekly intervals.
- Maximum dose – 20 mg/kg capped at 1000 mg/week.

### Administration

- Dilute using 0.9% sodium chloride:
  - maximum concentration 5 mg/mL
  - minimum concentration 2 mg/mL.
- For children under 14 years of age, use a maximum dose of 20 mg/kg/week, and round down to the nearest ampoule (to a maximum of 1000 mg/week).
- Administer over at least 15 minutes.

**Table D.1 Total dose (mg of IV iron carboxymaltose) based on Hb concentration and body weight**

| DOSES ARE IN mg | BODY WEIGHT (kg) | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Hb (g/L) | 35 | 40 | 45 | 50 | 55 | 60 | 65 | 70 | 75 | 80 |
| 60 | 1200 | 1300 | 1400 | 1500 | 1600 | 1700 | 1900 | 2100 | 2200 | 2300 |
| 75 | 1100 | 1200 | 1300 | 1400 | 1400 | 1500 | 1600 | 1800 | 1900 | 2000 |
| 90 | 1000 | 1000 | 1100 | 1200 | 1200 | 1300 | 1400 | 1600 | 1600 | 1700 |
| 105[b] | 800 | 900 | 900 | 1000 | 1000 | 1100 | 1200 | 1300 | 1400 | 1400 |
| **Maximum dose/ week[a]** | **700** | **800** | **900** | **1000** | **1000** | **1000** | **1000** | **1000** | **1000** | **1000** |

Hb, haemoglobin; IV, intravenous
[a] Maximum dose is 20 mg/kg (to a maximum of 1000 mg/week).
[b] Pink shading indicates that the infusion can be given in a single dose; in all other instances, the dose needs to be split over more than 1 week.
Source: Royal Children's Hospital, Melbourne (2013)[29]

The use of Ferinject in children constitutes an "off label" use of this product. Product Information approved by the Australian Therapeutic Goods Administration for Ferinject provides that the use of Ferinject has not been studied in children and therefore is not recommended in children under 14 years. However, the information in these Guidelines refers to best available evidence[36] and current clinical practice protocols[29] that support the safety and efficacy of this product for paediatric use. When considering these Guidelines, clinicians should use their professional judgement to consider this evidence, taking into account the preferences of the individual or their carer.

## D3 Iron sucrose (Venofer) dose[30]

### Presentation

- Ampoule of 5 mL is equivalent to 100 mg of iron (i.e. 20 mg/mL).

### Maximum dose

- Maximum dose per infusion is 7 mg/kg of iron (0.35 mL/kg) capped at 300 mg (15 mL).
- This maximum dose is suitable for iron deficiency anaemia, lower doses may be appropriate in maintenance therapy in chronic kidney disease.

## Table D.2 Total dose (mL of IV iron sucrose) based on Hb concentration and body weight

| DOSES ARE IN mL (20 mg/mL solution) | | BODY WEIGHT (kg) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hb (g/L) | | 5 | 10 | 15 | 20 | 25 | 30 | 35 | 40 | 45 | 50 | 55 | 60 | 65 | 70 |
| 60 | | 8 | 16 | 24 | 32 | 40 | 48 | 63 | 68 | 74 | 79 | 84 | 90 | 95 | 101 |
| 75 | | 7 | 14 | 21 | 28 | 35 | 42 | 57 | 61 | 66 | 70 | 75 | 79 | 84 | 88 |
| 90 | | 6 | 12 | 19 | 25 | 31 | 37 | 50 | 54 | 57 | 61 | 65 | 68 | 72 | 75 |
| 105 | | 5 | 11 | 16 | 21 | 26 | 32 | 44 | 47 | 49 | 52 | 55 | 57 | 60 | 63 |
| Max dose/ infusion[a] | mL | 1.75 | 3.5 | 5.25 | 7.0 | 8.75 | 10.5 | 12.25 | 14 | 15 | 15 | 15 | 15 | 15 | 15 |
| | mg | 35 | 70 | 105 | 140 | 175 | 210 | 245 | 280 | 300 | 300 | 300 | 300 | 300 | 300 |

Hb, haemoglobin; IV, intravenous
[a] Maximum dose per infusion is 7 mg/kg (to a maximum of 300 mg).[31]
Source: Royal Children's Hospital, Melbourne (2012)[30]

### Administration

To calculate the number of doses to be given, divide the total dose of IV iron sucrose in the upper part of the table by the maximum dose of IV iron sucrose per infusion (in mL) in the lower part of the table. Do not give more than three doses per week.

### Children (>1 month of age):

- For body weight 5–10 kg, dilute doses <100 mg 1:1 with normal saline, infuse over 30 minutes.
- For body weight 15–25 kg, dilute doses 100–200 mg in 200 mL normal saline, infuse over 60 minutes.
- For body weight 30–70 kg, dilute doses 200–300 mg in 300 mL normal saline, infuse over 90 minutes.

The use of Venofer in children constitutes an "off label" use of this product. Product Information approved by the Australian Therapeutic Goods Administration for Venofer provides that the safety and efficacy of Venofer in children has not been established. However, the information in these Guidelines refers to best available evidence[31] and current clinical protocol[30] that support the safety and efficacy of this product for paediatric use. When considering these Guidelines, clinicians should use their professional judgement to consider this evidence, taking into account the preferences of the individual or their carer.

# D4 Iron polymaltose (Ferrosig) dose[32]

### Presentation

- Ampoule = 2 mL of iron polymaltose = 100 mg of iron.

### Dose

- See Table D.3. None of the doses in the table exceed the recommended maximum dose of 2500 mg/infusion.

### Administration

- Dilute with 0.9% sodium chloride to a maximum concentration of 5 mg/mL.
- Standard infusion (500 mL 0.9% saline):
  - commence infusion at 40 mL/hour for 75 minutes (50 mL)
  - then increase by 20 mL/hour 15 minutely to a maximum rate of 120 mL/hour.
- For smaller patients or fluid restricted (250 mL 0.9% saline):
  - commence infusion at 20 mL/hour for 75 minutes (25 mL)
  - then grade up by 10 mL/hour to a maximum rate of 60 mL/hour.

**Table D.3 Dose (mL of IV iron polymaltose) based on Hb concentration and body weight**

| DOSES ARE IN mL (100mg/2mL or 50mg/mL solution)[a] | BODY WEIGHT (kg) | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Hb (g/L) | 5 | 10 | 15 | 20 | 25 | 30 | 35 | 40 | 45 | 50 | 55 | 60 | 65 | 70 |
| 60 | 3 | 6 | 10 | 13 | 16 | 19 | 25 | 27 | 30 | 32 | 34 | 36 | 38 | 40 |
| 75 | 3 | 6 | 9 | 11 | 14 | 17 | 23 | 24 | 26 | 28 | 30 | 32 | 33 | 35 |
| 90 | 3 | 5 | 7 | 10 | 12 | 15 | 20 | 22 | 23 | 24 | 26 | 27 | 29 | 30 |
| 105 | 2 | 4 | 6 | 8 | 11 | 13 | 18 | 19 | 20 | 21 | 22 | 23 | 24 | 25 |

Hb, haemoglobin; IV, intravenous
[a] Maximum dose 2500 mg/infusion
Source: Royal Children's Hospital, Melbourne (2012)[32]

### Administration

- Use Hb closest to patient's Hb.
- Doses coloured blue may be diluted in 250 mL of 0.9% sodium chloride.
- Doses coloured red may be diluted in 500 mL of 0.9% sodium chloride.
- Doses coloured purple need dilution in 1000 mL of 0.9% sodium chloride.

# Critical bleeding protocol for infants and children

This template, developed by consensus, covers areas that should be included in a critical bleeding protocol.
The template can be adapted to meet the local institution's patient population and resources.

**Senior clinician** determines that patient meets criteria for critical bleeding protocol activation

**'Activate critical bleeding protocol'**

## Baseline

Full blood count, blood group and cross match, coagulation screen (PT, APTT and fibrinogen), biochemistry, arterial blood gas and POC testing (if available)

**Notify transfusion laboratory** *(insert contact no.)*

## Roles

**Senior clinician**

- Coordinate team and allocate roles
- Determine volume and type of product, guided by clinical findings, estimated weight laboratory results and, if available, POC testing
- Consult haematologist/transfusion specialist as needed

**Laboratory staff**

- Notify haematologist or transfusion specialist
- Prepare and issue blood components
- Anticipate testing and blood component requirements
- Minimise test turnaround times
- Consider staff resources

**Haematologist or transfusion specialist**

- Support the clinical and laboratory staff as required

**Senior clinician to request critical bleeding protocol pack according to estimated weight**

- Packs should include RBC *Insert other components (e.g. FFP, platelets and cryoprecipitate, or fibrinogen concentrate) according to the locally agreed protocol.*
- Consider tranexamic acid in trauma patients

**Bleeding controlled?**

YES

NO

**Notify transfusion laboratory to:**
**'Cease critical bleeding protocol'**

## OPTIMISE:

- oxygenation
- cardiac output
- tissue perfusion
- metabolic state

## MONITOR (every 30–60 mins):

- full blood count
- coagulation screen
- ionised calcium
- arterial blood gases

## AIM FOR:

- temperature >36°C
- pH >7.2
- lactate <4 mmol/L
- ionised calcium >1.1 mmol/L
- platelets >50 × $10^9$/L
- PT/APTT <1.5 × normal
- fibrinogen >2 g/L

# Suggested criteria for activation of critical bleeding protocol

- Actual or anticipated losses of >35–40 mL/kg of RBC in <4 hours, + haemodynamically unstable, ±anticipated ongoing bleeding
- Severe thoracic, abdominal, pelvic or multiple long bone trauma, and head trauma
- Major gastrointestinal or surgical bleeding

## Damage control resuscitation

- Identify cause and aggressively control bleeding
  - Compression, packing and tourniquet
  - Early surgical assessment and intervention
  - Angiography as needed
- Restore or maintain normal coagulation
- Avoid hypothermia (use active warming measures)
- Avoid excess crystalloid
- Tolerate permissive hypotension until bleeding is actively controlled
- Do not use haemoglobin alone as transfusion trigger

## Cell salvage

Consider use of cell salvage where appropriate

## Dosage

Optimise the use of each unit to minimise wastage

| | |
|---|---|
| RBC | 20–25 mL/kg |
| Platelet count <50 × $10^9$/L | platelets 10–15 mL/kg |
| PT/APTT >1.5 × normal | FFP 15 mL/kg[a] |
| Fibrinogen <2 g/L | Cryoprecipitate 5 mL/kg[a] |
| Tranexamic acid | Loading dose 15 mg/kg (max 1 g) over 10 min, then infusion 2 mg/kg/hour for 8 or more hours, or until bleeding ceases |

[a] Local transfusion laboratory to advise dose of locally available preparation

## Prevention of hypofibrinogenaemia

- Fibrinogen levels are reduced to a greater degree than other factors in large-volume bleeding. Dilution and hyperfibrinolysis (e.g. in trauma) further exacerbate low levels.
- In critical bleeding, maintaining fibrinogen at levels >2 g/L is suggested.
- Include guidance for the use and timing of fibrinogen replacement in the protocol; this may include viscoelastometric POC testing.

## Special clinical situation

Warfarin:

- add vitamin K, prothrombinex/FFP

Head injury:

- aim for platelet count >100 × $10^9$/L
- permissive hypotension contraindicated

## Considerations for use of rFVIIa[a]

Based on evidence from studies in adults, the *routine* use of rFVIIa in trauma patients is not recommended. However, institutions may choose to develop a process for the use of rFVIIa where the following apply:

- uncontrolled haemorrhage in salvageable patient, **and**
- failed surgical or radiological measures to control bleeding, **and**
- adequate blood component replacement, **and**
- pH >7.2, temperature >34 °C.

Discuss dose with haematologist or transfusion specialist

[a] rFVIIa is not licensed for use in this situation; all use must be part of practice review.

APTT, activated partial thromboplastin time; FFP, fresh frozen plasma; INR, international normalised ratio; POC, point of care; PT, prothrombin time; RBC, red blood cell; rFVIIa, activated recombinant factor VII

This appendix provides guidance from the Clinical/Consumer Reference Group (CRG) on tranexamic acid (TXA) dosing in various paediatric patient groups. Evidence for appropriate paediatric dosing is available for craniofacial surgery,[33] and pragmatic dosing regimens are suggested for trauma[34] and scoliosis surgery,[35] but not for cardiac surgery, as explained below.

# E1 Surgery other than cardiac

**Table E.1 Guidance on tranexamic dosing in surgical paediatric patients other than cardiac**

| PATIENT GROUP | LOADING DOSE (mg/kg over 10 minutes, up to a maximum of 1 g) | INFUSION (mg/kg/hour) |
|---|---|---|
| Trauma[a] | 15 | 2 |
| Craniofacial surgery | 10 | 5 |
| Scoliosis surgery | 10 | 5 |

[a] Commencing within 3 hours of trauma and continuing for at least 8 hours or until bleeding stops.

# E2 Cardiac surgery

There is a lack of evidence for appropriate target plasma concentrations for TXA in paediatric cardiac surgery; hence, no specific guidance on dosing can be given for this patient group. However, a safe and effective dose regimen is likely to need to take into account factors such as age, weight, pump prime volume and use of ultrafiltration. A loading dose followed by a continuous infusion is more likely than intermittent boluses to produce stable plasma concentrations.[20]

# Appendix F Critical bleeding protocol

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