Patient Blood Management Guidelines: Module 4

Critical Care

Quick Reference Guide

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Disclaimer

This document is a general guide to appropriate practice, to be followed subject to the circumstances, clinician's judgement and patient's preferences in each individual case. It is designed to provide information to assist decision making. Recommendations contained herein are based on the best available evidence published up to July 2010 (Question 1), September 2010 (Questions 2 and 3) and March 2011 (Question 4). The relevance and appropriateness of the information and recommendations in this document depend on the individual circumstances. Moreover, the recommendations and guidelines are subject to change over time.

Each of the parties involved in developing this document expressly disclaims and accepts no responsibility for any undesirable consequences arising from relying on the information or recommendations contained herein.

Patient Blood Management Guidelines: Module 4 – Critical Care

Development of this quick reference guide was achieved through clinical input and expertise of representatives from the colleges and societies listed below and a patient blood management advocate (see Appendix A in the Module).

Australian and New Zealand College of Anaesthetists

Australian and New Zealand Intensive Care Society

College of Intensive Care Medicine of Australia and New Zealand

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

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AUSTRALIA

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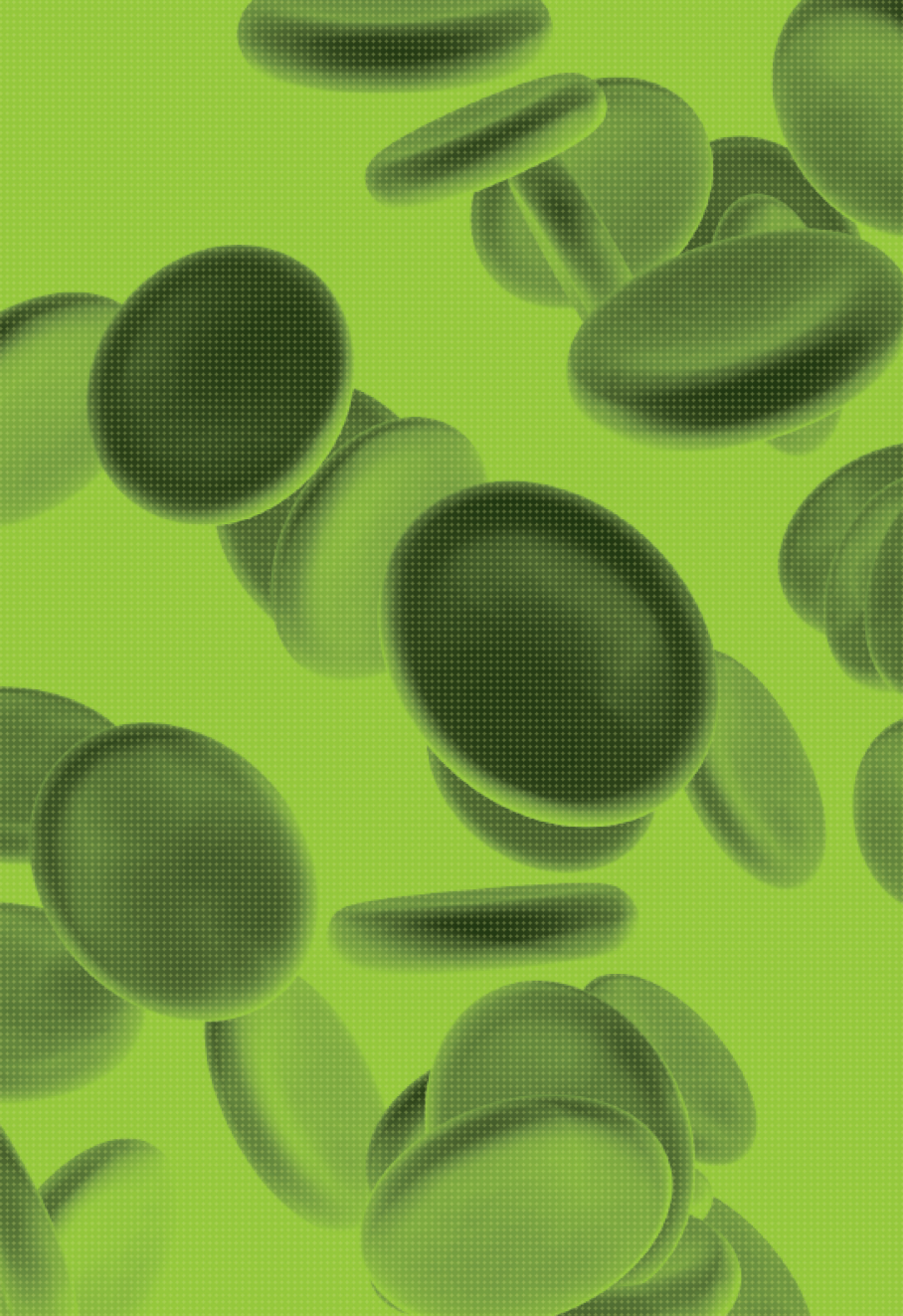
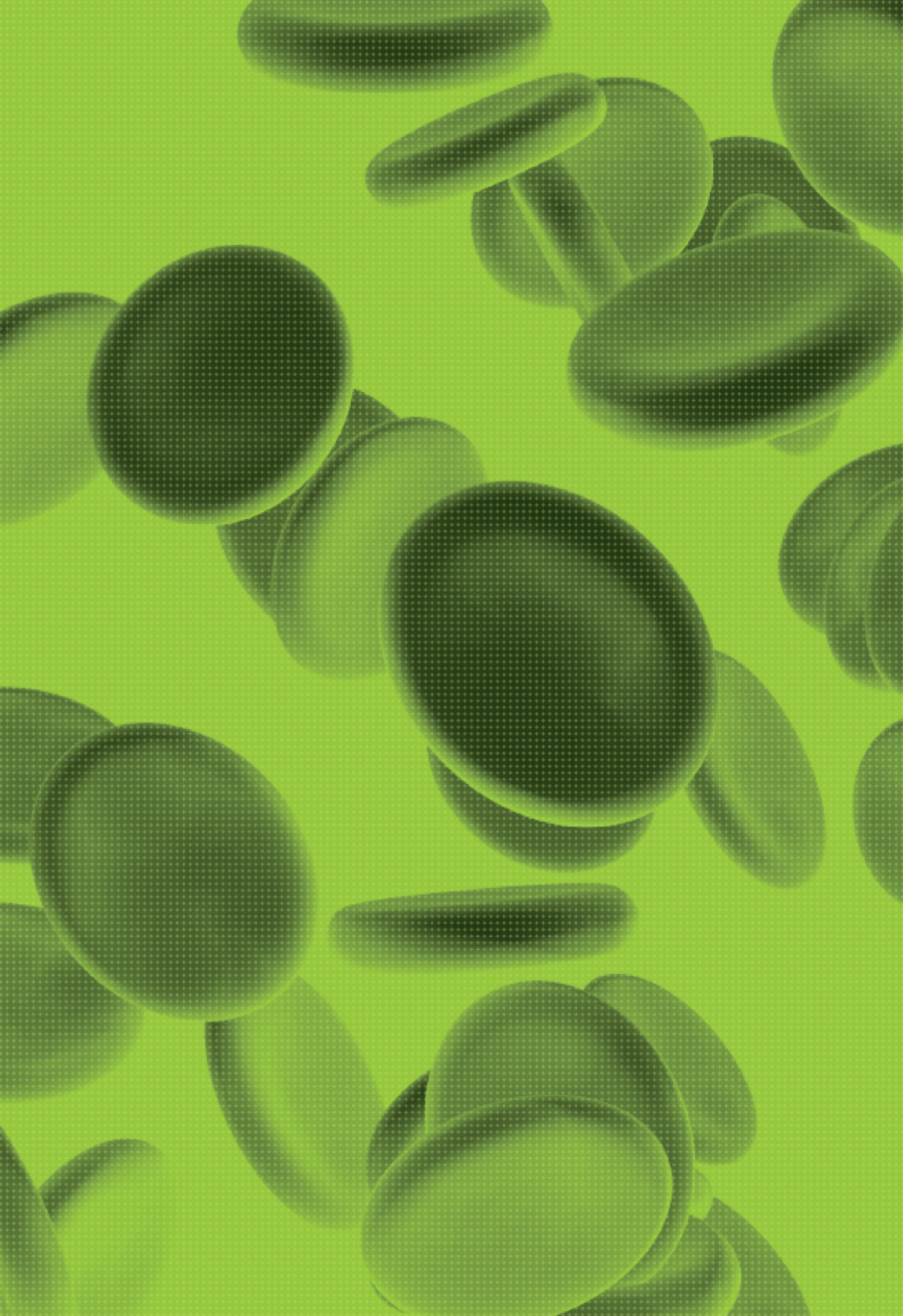


Abbreviations and acronyms

ACS	acute coronary syndrome
ALI	acute lung injury
ARDS	acute respiratory distress syndrome
ASBT	Australasian Society of Blood Transfusion
CRASH	Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage
CRG	Clinical/Consumer Reference Group
ESA	erythropoiesis-stimulating agent
FFP	fresh frozen plasma
GI	gastrointestinal
Hb	haemoglobin
ICU	intensive care unit
INR	international normalised ratio
MI	myocardial infarction
NBA	National Blood Authority
NHMRC	National Health and Medical Research Council
PP	practice point
R	recommendation
RBC	red blood cell
RCT	randomised controlled trial
TXA	tranexamic acid



Contents

1. Introduction

The Patient Blood Management Guidelines: Module 4 – Critical Care[1] (*Module 4 – Critical Care*), is the fourth in a series of six modules that focus on evidence-based patient blood management. The other five modules are critical bleeding/massive transfusion, perioperative, medical, obstetrics and paediatrics/neonates. Together, Module 2 – Perioperative and Module 3 – Medical cover all the patient groups addressed by the 2001 document *Clinical Practice Guidelines on the Use of Blood Components*[2] (National Health and Medical Research Council/Australasian Society of Blood Transfusion, NHMRC/ASBT). Thus, the 2001 guidelines have now been replaced.

Module 4 – Critical Care 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 4 – Critical Care includes:

- a summary of the *recommendations* that were developed by the CRG, based on evidence from a systematic review
- a summary of the *practice points* that were developed by the CRG through consensus decision making

Details of the systematic reviews used in the development of Module 4 – Critical Care, for which the electronic searches included articles published between 1966 and July 2010 (Question 1), September 2010 (Questions 2 and 3) and March 2011 (Question 4), are given in the technical reports[3,4] available on the National Blood Authority (NBA) website.

2. Development of recommendations and practice 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.

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

3. Categorisation of recommendations and practice 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 4 – Critical Care, where references are provided.

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

ELEMENT OF PATIENT BLOOD MANAGEMENT	RECOMMENDATION	PRACTICE POINT	RELEVANT SECTION OF THIS QUICK REFERENCE GUIDE	RELEVANT SECTION OF MODULE 4 – CRITICAL CARE
Non-transfusion interventions				
Erythropoiesis-stimulating agents	R2	-	4.2	3.2
Appropriate transfusion practices				
Red blood cells	R1	PP1-4	4.1	3.1
Fresh frozen plasma	-	PP5-7	4.3	3.3.1
Fibrinogen concentrate and cryoprecipitate	-	PP8-9	4.4	3.2.2
Platelets	-	PP10-12	4.5	3.3.3
Blood conservation strategies				
Cell salvage	-	PP13	4.6	3.4.1
Tranexamic acid	R3, R4	PP14-15	4.7	3.4.2

4. Recommendations and practice points

4.1 Red blood cells

RECOMMENDATION - red blood cells	
R1 **GRADE B**	In critically ill patients, a restrictive transfusion strategy should be employed (Grade B).

PRACTICE POINTS - red blood cells	
PP1	RBC transfusion should not be dictated by a Hb concentration alone, but should also be based on assessment of the patient's clinical status.
PP2	Where indicated, 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.
PP3	CRG consensus suggests that, with a: ▪ **Hb concentration <70 g/L,** RBC transfusion is likely to be appropriate; however, transfusion may not be required in well-compensated patients or where other specific therapy is available. ▪ **Hb concentration of 70–90 g/L**, RBC transfusion is not associated with reduced mortality. The decision to transfuse patients (with a single unit followed by reassessment) should be based on the need to relieve clinical signs and symptoms of anaemia. ▪ **Hb concentration >90 g/L**, RBC transfusion is generally unnecessary. For patients undergoing cardiac surgery, refer to *Patient Blood Management Guidelines: Module 2 – Perioperative;*[5] for patients with active bleeding, refer to *Patient Blood Management Guidelines: Module 1 – Critical Bleeding/ Massive Transfusion.*[6]

PP4	For patients with ACS, the following guidance is taken from *Patient Blood Management Guidelines: Module 3 – Medical*.[7] In ACS patients with a: ▪ **Hb concentration <80 g/L**, RBC transfusion may be associated with reduced mortality and is likely to be appropriate (see PP5 of Module 3). ▪ **Hb concentration of 80–100 g/L**, the effect of RBC transfusion on mortality is uncertain and may be associated with an increased risk of recurrence of MI (see PP6 of Module 3). ▪ **Hb concentration >100 g/L**, RBC transfusion is not advisable because of an association with increased mortality (see R1 of Module 3). Any decision to transfuse should be made with caution and based on careful consideration of the risks and benefits (see PP6 of Module 3).

ACS, acute coronary syndrome; CRG, Clinical/Consumer Reference Group; Hb, haemoglobin; MI, myocardial infarction; PP, practice point; R, recommendation; RBC, red blood cell

4.2 Erythropoiesis-stimulating agents

RECOMMENDATION - erythropoiesis-stimulating agents	
R2 **GRADE B**	ESAs should not be routinely used in critically ill anaemic patients (Grade B).[a]

ESA, erythropoiesis-stimulating agent; R, recommendation

[a] This recommendation is based on the lack of effect of ESAs on mortality in a heterogeneous population of critically ill patients.

4.3 Fresh frozen plasma

PRACTICE POINTS – fresh frozen plasma	
PP5	The routine use of FFP in critically ill patients with coagulopathy is not advised. The underlying causes of coagulopathy should be identified.
PP6	The administration of FFP may be independently associated with adverse events, including ARDS and ALI. The decision to transfuse these products to an individual patient should take into account the relative risks and benefits.
PP7	Assessment of bleeding risk is complex and requires careful consideration of patients' clinical status and laboratory parameters. Specialist haematology advice may also be required. However, patients with an INR ≤2 may not benefit from the administration of FFP and can generally undergo invasive procedures within the ICU without any serious bleeding; higher INRs may be tolerated in certain clinical situations.

ALI, acute lung injury; ARDS, acute respiratory distress syndrome; FFP, fresh frozen plasma; ICU, intensive care unit; INR, international normalised ratio; PP, practice point

4.4 Fibrinogen concentrate and cryoprecipitate

PRACTICE POINTS – fibrinogen concentrate and cryoprecipitate	
PP8	The routine use of cryoprecipitate and fibrinogen concentrate in critically ill patients with coagulopathy is not advised. The underlying causes of coagulopathy should be identified.
PP9	The effect of cryoprecipitate and fibrinogen on transfusion-related serious adverse events is uncertain. The decision to transfuse cryoprecipitate or fibrinogen to an individual patient should take into account the relative risks and benefits.

PP, practice point

4.5 Platelet transfusion

PRACTICE POINTS – platelet transfusion	
PP10	The effect of platelet transfusion on transfusion-related serious adverse events is uncertain. The decision to transfuse platelets to an individual patient should take into account the relative risks and benefits.
PP11	In critically ill patients, in the absence of acute bleeding, the administration of platelets may be considered appropriate at a platelet count of $<20 \times 10^9$/L.
PP12	Assessment of bleeding risk is complex and requires careful consideration of patients' clinical status and laboratory parameters. Specialist haematology advice may also be required. However, patients with a platelet count $\geq 50 \times 10^9$/L can generally undergo invasive procedures within the ICU without any serious bleeding; lower platelet counts may be tolerated in certain clinical situations.

ICU, intensive care unit; PP, practice point

4.6 Cell salvage

PRACTICE POINT – cell salvage	
PP13	In critically ill trauma patients and patients undergoing emergency surgery for ruptured abdominal aortic aneurysm, the use of cell salvage may be considered.

PP, practice point

4.7 Tranexamic acid

RECOMMENDATIONS – tranexamic acid	
R3 **GRADE B**	In acutely bleeding critically ill trauma patients, TXA should be administered within 3 hours of injury (Grade B).
R4 **GRADE C**	In critically ill patients with upper GI bleeding, consider the use of TXA (Grade C).

PRACTICE POINTS – tranexamic acid	
PP14	TXA should be given as early as possible, preferably within 3 hours of injury. The late administration of TXA is less effective and may be harmful.
PP15	The suggested dose of TXA administered is a 1 g bolus followed by a 1 g infusion over 8 hours. This is the dose administered in the large multicentre RCT CRASH-2.

CRASH, Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage; GI, gastrointestinal; PP, practice point; R, recommendation; RCT, randomised controlled trial; TXA, tranexamic acid

5. Massive transfusion protocol (MTP) template

The MTP template is given below. This section discusses local adaptation of the template MTP, and development of guidelines on activation and cessation of the MTP.

5.1 Local adaptation

A multidisciplinary team should adapt the MTP template to:

- incorporate the recommendations and practice points provided in *Module 1 – Critical Bleeding/Massive Transfusion*
- take into account local resources (e.g. access to blood components)
- provide details of how components will be delivered to the correct patient and location
- include supporting information that explains how the clinical, laboratory and support staff will communicate
- highlight the need for early communication with a haematologist or transfusion specialist.

The MTP template can also be modified for specific populations such as obstetric patients, given the potential for concealed haemorrhage and early development of disseminated intravascular coagulation.

The local facility should also develop materials to accompany the MTP, clarifying the roles and responsibilities of the team members (e.g. task cards).

5.2 Activation and cessation

The multidisciplinary team should also develop guidelines for the activation and cessation of the MTP. This will help to ensure that the MTP is used appropriately, and wastage of blood components is minimised.

Activation of the MTP should take into account:

- cause and rate of the haemorrhage
- mechanism of injury (if present)
- current physiological state
- likely requirement for ongoing blood component support.

The MTP template given here includes suggestions on when to activate an MTP. The guidelines on activation and cessation of the MTP should be clearly communicated to all relevant staff.

Use of the MTP should be audited.

Massive transfusion protocol (MTP) template

Senior clinician determines that patient meets criteria for MTP activation

Baseline:

Full blood count, coagulation screen (PT, INR, APTT, fibrinogen), biochemistry, arterial blood gases

Notify transfusion laboratory *(insert contact no.)* **to:**
'Activate MTP'

Laboratory staff

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

Haematologist/transfusion specialist

- Liaise regularly with laboratory and clinical team
- Assist in interpretation of results, and advise on blood component support

Senior clinician

- **Request:**[a]
  - 4 units RBC
  - 2 units FFP
- **Consider:**[a]
  - 1 adult therapeutic dose platelets
  - tranexamic acid in trauma patients
- **Include:**[a]
  - cryoprecipitate if fibrinogen < 1 g/L

[a] Or locally agreed configuration

Bleeding controlled?

YES / **NO**

Notify transfusion laboratory to:
'Cease MTP'

This information, developed by consensus, broadly covers areas that should be included in a local MTP.

This template can be used to develop an MTP to meet the needs of the local institution's patient population and resources.

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 > 35ºC
- pH > 7.2
- base excess < – 6
- lactate < 4 mmol/L
- Ca^{2}+ > 1.1 mmol/L
- platelets > 50 x 10^{9}/L
- PT/APTT < 1.5 x normal
- INR ≤1.5
- fibrinogen > 1.0 g/L

*The numerical representation of base excess can be shown differently in varying texts. Please be aware that for the purposes of this template, a base excess of <-6 refers to a base excess of -5, -4, -3 and so forth. A base excess of -7, -8, -9 and so on is associated with a worsening prognosis. The normal range for base excess is -2 - +2.

Suggested criteria for activation of MTP

- **Actual or anticipated 4 units RBC in < 4 hrs, + haemodynamically unstable, +/– anticipated ongoing bleeding**
- **Severe thoracic, abdominal, pelvic or multiple long bone trauma**
- **Major obstetric, gastrointestinal or surgical bleeding**

Initial management of bleeding

- Identify cause
- Initial measures:
  - compression
  - tourniquet
  - packing
- Surgical assessment:
  - early surgery or angiography to stop bleeding

Specific surgical considerations

- If significant physiological derangement, consider damage control surgery or angiography

Cell salvage

- Consider use of cell salvage where appropriate

Dosage

Platelet count < 50 x 10^9/L	1 adult therapeutic dose
INR > 1.5	FFP 15 mL/kg[a]
Fibrinogen < 1.0 g/L	cryoprecipitate 3–4 g[a]
Tranexamic acid	loading dose 1 g over 10 min, then infusion of 1 g over 8 hrs

[a] Local transfusion laboratory to advise on number of units needed to provide this dose

This information, developed by consensus, broadly covers areas that should be included in a local MTP.
This template can be used to develop an MTP to meet the needs of the local institution's patient population and resources.

Resuscitation

- Avoid hypothermia, institute active warming
- Avoid excessive crystalloid
- Tolerate permissive hypotension (BP 80–100 mmHg systolic) until active bleeding controlled
- Do not use haemoglobin alone as a transfusion trigger

Special clinical situations

- Warfarin:
  - add vitamin K, prothrombinex/FFP
- Obstetric haemorrhage:
  - early DIC often present; consider cryoprecipitate
- Head injury:
  - aim for platelet count > 100 x 10^9/L
  - permissive hypotension contraindicated

Considerations for use of rFVIIa[b]

The *routine* use of rFVIIa in trauma patients is not recommended due to its lack of effect on mortality (Grade B) and variable effect on morbidity (Grade C). Institutions may choose to develop a process for the use of rFVIIa where there is:

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

Discuss dose with haematologist/transfusion specialist

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

ABG	arterial blood gas
FFP	fresh frozen plasma
APTT	activated partial thromboplastin time
INR	international normalised ratio
BP	blood pressure
MTP	massive transfusion protocol
DIC	disseminated intravascular coagulation
PT	prothrombin time
FBC	full blood count
RBC	red blood cell
rFVIIa	activated recombinant factor VII

6. 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).

7. References

1. National Blood Authority (NBA) (2013). *Patient blood management guidelines: Module 4 – Critical care*. NBA, Canberra, Australia.

2. National Health and Medical Research Council (NHMRC) and Australasian Society of Blood Transfusion (ASBT) (2001). *Clinical practice guidelines on the use of blood components*, NHMRC, Canberra, Australia http://www.nhmrc.gov.au/guidelines/publications/cp78

3. National Blood Authority (NBA) (2013). *Technical report on critical care patient blood management: Volume 1 – Review of the evidence*. NBA, Canberra, Australia.

4. National Blood Authority (NBA) (2013). *Technical report on critical care patient blood management: Volume 2 – Appendixes*. NBA, Canberra, Australia.

5. National Blood Authority (NBA) (2012). *Patient blood management guidelines: Module 2 – Perioperative*. NBA, Canberra, Australia.

6. National Blood Authority (NBA) (2011). *Patient blood management guidelines: Module 1 – Critical bleeding/Massive transfusion*. NBA, Canberra, Australia.

7. National Blood Authority (NBA) (2012). *Patient blood management guidelines: Module 3 – Medical*. NBA, Canberra, Australia.