

From the Chief Medical Officer
Dr Michael McBride

HSS(MD) 22/2012

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Dear Colleague

DETECTION, INVESTIGATION AND MANAGEMENT OF ANAEMIA

1. The purpose of this letter is to disseminate two new guidance documents on the detection, investigation and management of anaemia. The documents are:
 - i. **FOUR STEPS IN THE INVESTIGATION AND MANAGEMENT OF THE ADULT PATIENT WITH ANAEMIA**
 - ii. **MANAGEMENT OF THE ANAEMIC ADULT PATIENT PRIOR TO SCHEDULED MAJOR SURGERY**



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BACKGROUND

2. Detection, investigation and management of anaemia play an important part not only in improving the care and outcome for the patient, but also in reducing the need for blood transfusion. In order to address these two issues, the Northern Ireland Transfusion Committee (NITC) has developed this guidance through consultation with a range of healthcare professionals in primary and secondary care. The final documents have been endorsed by the Advisory Committee on Blood Safety for publication.

FOUR STEPS IN THE INVESTIGATION AND MANAGEMENT OF THE ADULT PATIENT WITH ANAEMIA

3. This guidance clearly sets out the appropriate actions required for investigation and management of patients in each of the main categories of anaemia. The document is presented as a series of colour-coded algorithms which can be copied and displayed on wall boards and as on-line documents for ease of reference. The document can be found at Annex A.

MANAGEMENT OF THE ANAEMIC ADULT PATIENT PRIOR TO SCHEDULED MAJOR SURGERY

4. The aim of this guidance is to optimise haemoglobin and haemostasis prior to planned major surgery or other invasive procedures associated with blood loss. It sets out a recommended plan of management of the patient and details the actions required prior to major surgery taking place. This 2-page document is also presented in a format suitable for display on wall boards or on-line. The document can be found at Annex B.

ACTION REQUIRED

5. **Trust Chief Executives and/or Medical and Nursing Directors should ensure that these two guidance documents are disseminated to all clinicians, regardless of speciality. Trust Chief Executives should confirm receipt and dissemination of this guidance by return to irene.wilkinson@dhsspsni.gov.uk , secretariat for the Advisory Committee on Blood Safety.**
6. **All clinicians, regardless of specialty, should familiarise themselves with the content of these two guidance documents and begin to implement the actions immediately, with the aim of full implementation by the end of September 2012, as stated in BBT3. Trust Chief Executives should confirm implementation by end of September 2012. Responses to be sent to irene.wilkinson@dhsspsni.gov.uk , secretariat for the Advisory Committee on Blood Safety.**
7. **All GPs, including locums, should familiarise themselves with the content of these two guidance documents and begin to implement the actions immediately, with the aim of full implementation by the end of September 2012, as stated in Better Blood Transfusion 3 (BBT3).**

8. Clinicians in secondary and primary care should work together to address anaemia in patients as required.
9. Where appropriate this guidance should be included in pre and post-registration training and education programmes.

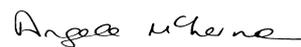
CONCLUSION

10. In conclusion we would like to thank Dr Susan Atkinson (Chair) and all members of the Northern Ireland Transfusion Committee for development of these clear and evidence based guidelines. We commend these to all clinicians and stress the benefit to patients when anaemia is detected, investigated and managed appropriately, particularly before scheduled major surgery. Implementation of the guidance should begin immediately, with the aim of full implementation by the end of September 2012, as stated in BBT3.

Yours sincerely



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Chief Medical Officer



MRS ANGELA MCLERNON
Acting Chief Nursing Officer

This letter is available on the DHSSPS website at
www.dhsspsni.gov.uk/index/phealth/professional/cmo_communications.htm

4 STEPS IN THE INVESTIGATION AND MANAGEMENT OF THE ADULT PATIENT WITH ANAEMIA

STEP 1

Perform FBP test for Hb, MCV and MCH

If patient anaemic as per * WHO Classification of anaemia follow steps below

* WHO Classification of anaemia

Haemoglobin: < 13 g/dl in adult male
< 12 g/dl in adult female
< 11 g/dl in pregnancy

STEP 2

MCV or MCH low: perform iron studies (including serum ferritin)

MCV & MCH normal range: perform iron studies & renal function tests, serum folate & vitamin B12 levels

MCV or MCH high: perform LFTs, thyroid function, serum folate and vitamin B12 levels

Abbreviations used:

FBP: full blood picture

Hb: Haemoglobin

MCV: Mean corpuscular volume

MCH: Mean corpuscular haemoglobin

WCC: white blood cell count

CRP: C-reactive protein

TIBC: total iron binding capacity

TSAT: transferrin saturation

LFTs: liver function tests

ESA: erythrocyte stimulating factor or recombinant erythropoietin

eGFR: estimated glomerulofiltration rate

CKD: chronic kidney disease

STEP 3

1. Start appropriate corrective therapy for anaemia without delay (e.g. oral iron therapy)

AND

2. Investigate cause of anaemia unless already known or further investigation is not in the patient's best interests (e.g. palliative care only)

Sickle cell disease – perform Sickledex test if positive family history or patient's genetic origin is West Africa

STEP 4

1. Monitor response to corrective therapy for anaemia, including rise in Hb

AND

2. Treat the cause of anaemia (e.g. surgery for carcinoma of bowel)

4 STEPS IN THE INVESTIGATION AND MANAGEMENT OF THE ADULT PATIENT WITH ANAEMIA
MICROCYTIC ANAEMIA

** Normal range values may differ between hospital laboratories

** MCV < 76fl or MCH < 27pg
 Microcytic anaemia

STEP 1
 • Full Blood Picture Test

STEP 2
 • Iron studies (include se ferritin and TIBC or TSAT)
 • CRP

STEP 3:
 • Correct anaemia
 • Investigate cause if unknown (unless further investigation is not in the patient's best interests)

STEP 4:
 • Monitor response to replacement therapy
 • Treat disease causing the anaemia

Se ferritin < 30 mcg/l when CRP < 30 mg/l
 Se ferritin < 70 mcg/l when CRP > 30 mg/l
 TIBC increased or TSAT <20%
 Manage as IRON DEFICIENCY ANAEMIA

Se ferritin > 70 mcg/l, CRP normal or increased
 TIBC normal or decreased, TSAT > 20%
 Go to STEP 3

IRON DEFICIENCY ANAEMIA

a) Start oral iron therapy to normalise Hb and replenish iron stores
 Start with parenteral iron therapy if:
 - History of oral iron intolerance or poor compliance
 - Impaired gastrointestinal absorption
 - Haemodialysis
 - Major surgery must take place in < 3 weeks

b) Review history & examination for source of chronic bleeding
 Refer to gastroenterologist if
 - Adult male
 - Postmenopausal female
 - Premenopausal female with gastro-intestinal symptoms or bleeding

Refer to gynaecologist if
 - Post menopausal bleeding
 - Menorrhagia

MICROCYTIC ANAEMIA NOT DUE TO IRON DEFICIENCY

Assess for acute or chronic inflammatory disease, chronic infection, malignancy and liver disease – check differential WCC, LFTs

If thalassaemia or sideroblastic anaemia suspected or cause of anaemia unknown refer to a haematologist

IRON DEFICIENCY ANAEMIA

Perform FBP after 3 weeks of oral iron therapy
 If improvement in Hb (1-2 g/dl increase):
 - Check if Hb normalised after 2-4 months iron therapy
 - Continue iron therapy for another 3 months to replenish iron stores

If no improvement consider:
 - Switch to parenteral iron therapy

ANAEMIA OF CHRONIC DISEASE

A diagnosis of exclusion
 Unresponsive to parenteral iron unless iron deficiency also present

Treat and monitor the underlying cause

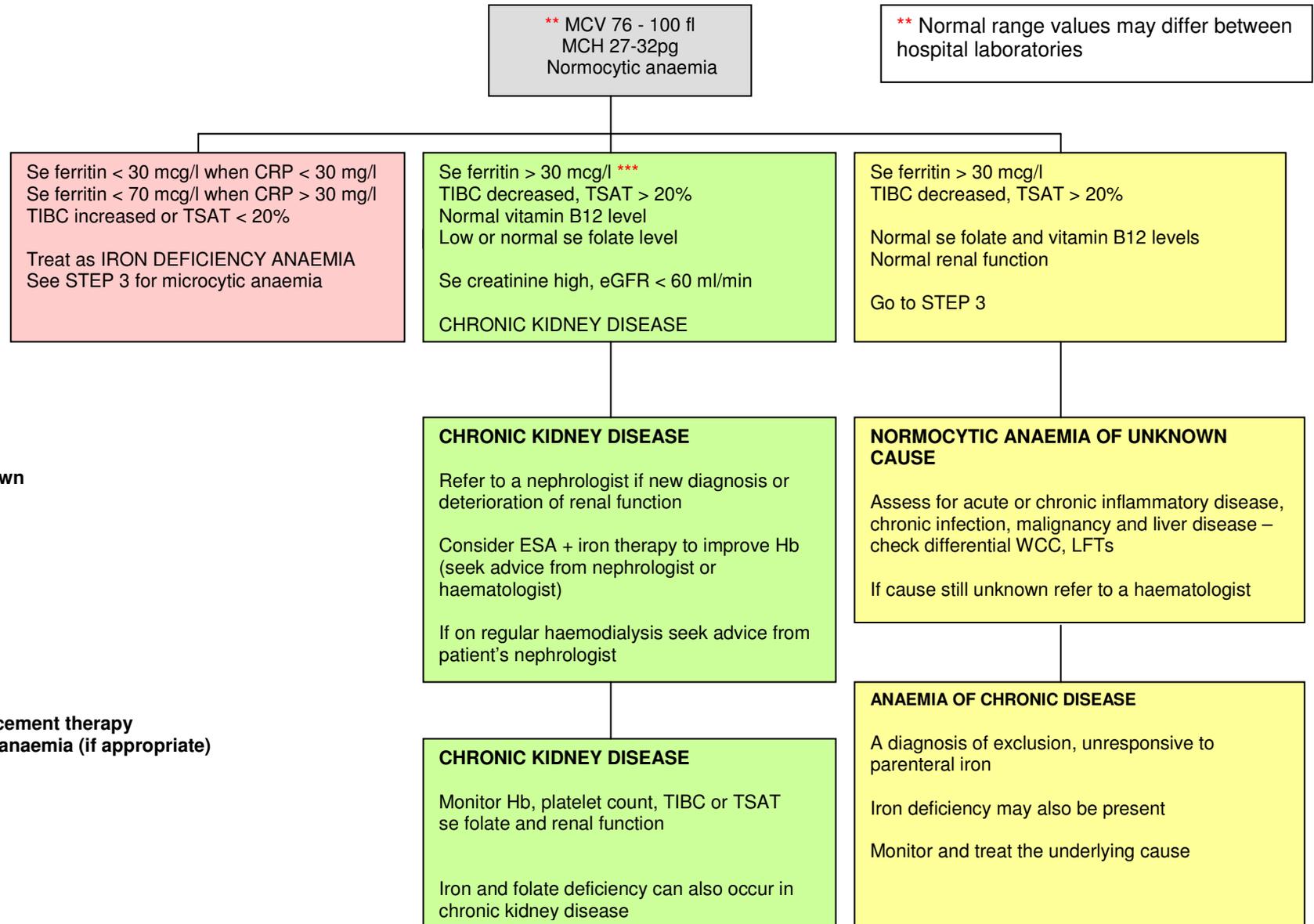
4 STEPS IN THE INVESTIGATION AND MANAGEMENT OF THE ADULT PATIENT WITH ANAEMIA
NORMOCYTIC ANAEMIA

STEP 1
 • Full Blood Picture Test

STEP 2
 • Iron studies (include se ferritin + TIBC or TSAT)
 • Se folate and vitamin B12
 • Urea, creatinine, eGFR

STEP 3:
 • Correct anaemia
 • Investigate cause if unknown

STEP 4
 • Monitor response to replacement therapy
 • Treat disease causing the anaemia (if appropriate)



4 STEPS IN THE INVESTIGATION AND MANAGEMENT OF THE ADULT PATIENT WITH ANAEMIA
MACROCYTIC ANAEMIA

STEP 1
 • Full Blood Picture Test

If haemolysis detected in FBP
 (confirmed on repeat testing)
 Refer to a haematologist

** MCV > 100 fl or
 MCH > 32 pg
 Macrocytic anaemia

** Normal range values may differ between
 hospital laboratories

STEP 2
 • Test se folate, vitamin B12
 • Urea, creatinine, eGFR
 • Liver function tests

Low se folate and / or low vitamin B12 level
**FOLATE AND / OR VITAMIN B12
 DEFICIENCY**

Normal renal function, se folate &
 B12 levels
 Go to STEP 3

STEP 3:
 • Correct anaemia
 • Investigate cause if unknown

FOLATE DEFICIENCY
 a. Start oral folic acid 5 mg daily
 If co-existing vitamin B12 deficiency start vitamin B12 injections at same time to avoid neurological complications
 b. Consider cause such as - poor diet, liver disease, alcohol misuse, gastro-intestinal surgery, recent pregnancy, chronic inflammatory disease (e.g. Crohn's disease or TB), malignancy and drug therapy (e.g. anticonvulsants)

VITAMIN B12 DEFICIENCY
 a. Hydroxocobalamin IM injections: 1 mg alternate days for 2 weeks, then 1 mg every 3 months for life
 b. Assess for malabsorption and consider post gastrectomy, terminal ileum disease or resection as cause

MACROCYTIC ANAEMIA OF UNKNOWN CAUSE
 Assess for liver disease, alcohol misuse, hypothyroidism and drug causes (e.g. cytotoxic therapy) of anaemia
 If myelodysplasia or myeloma suspected or if cause of anaemia still unknown refer to a haematologist

STEP 4
 • Monitor response to replacement therapy
 • Treat disease causing the anaemia

FOLATE INDUCED ANAEMIA
 Monitor Hb and reticulocyte count after 4 months replacement therapy
 Treat cause if identified

VITAMIN B12 DEFICIENCY INDUCED ANAEMIA
 Monitor Hb and reticulocyte count
 - after 10 days for response
 - after 8 weeks to check if Hb has returned to normal range

MACROCYTIC ANAEMIA not due to folate or vitamin B12 deficiency
 Monitor Hb
 Treat and monitor cause if identified

GUIDANCE ON THE INVESTIGATION AND MANAGEMENT OF THE ADULT PATIENT WITH ANAEMIA

Iron deficiency anaemia is the most prevalent cause of anaemia. It can be due to blood loss, impaired iron absorption or failure to utilise iron stores.

- 1. Have a high index of suspicion for iron deficiency anaemia** in patients with:
 - Chronic gastro-intestinal symptoms or evidence of chronic bleeding from gastro-intestinal tract
 - Acute or chronic inflammatory bowel disease or malabsorption
 - Malignancy
 - Menorrhagia
 - Pregnancy
- 2. Investigate the cause of anaemia promptly** unless the aetiology is already known or further investigations are not in the patient's best interests (e.g. palliative care patient).
Anaemia should be investigated more urgently in men with a haemoglobin concentration <12 g/dl and in women with a haemoglobin concentration <10 g/dl, because lower haemoglobin levels may be indicative of serious disease.
- 3. Once iron deficiency has been detected treatment should not be delayed**
 - Oral iron is the treatment of choice in most cases of iron deficiency anaemia.
 - Prescribe ferrous sulphate 200 mg twice or three times a day (at least 6 hr apart), preferably between meals if tolerated
 - Recommend ascorbic acid (vitamin C) 250 - 500 mg to be taken with the iron preparation to aid absorption, unless it induces gastro-intestinal irritation
 - If nausea, abdominal pain, constipation or diarrhoea occur, advise ferrous sulphate be taken with food or change to ferrous gluconate 600 mg twice a day.
 - Hb should rise by 1 - 2 g/dl every 3 weeks and be within normal range after 2 - 4 months of oral iron therapy.
 - Continue oral iron therapy for 3 months after haemoglobin has returned to normal range, to replenish iron stores.
 - Measure haemoglobin level every 3 months for a year and then after a year, prescribing additional iron as necessary.

Intravenous iron therapy is indicated if:

- Oral iron therapy has failed or not been tolerated
- History of malabsorption or active inflammatory bowel disease
- Functional iron deficiency – e.g. chronic kidney disease on haemodialysis
- Major surgery must proceed in less than 3 weeks time

Normocytic anaemia can be due to chronic kidney disease or anaemia of chronic disease (CKD) but may also be a sign of early iron deficiency anaemia.

*** In patients with stage 3 or 4 CKD and serum ferritin < 100 mcg/l, **consider presence of iron deficiency anaemia**

*** In patients with stage 5 CKD and serum ferritin < 100 mcg/l, **treat as iron deficiency anaemia**

Macrocytic anaemia is most commonly due to excessive alcohol intake, folate and / or vitamin B12 deficiency (megaloblastic anaemia) but may also occur with myelodysplasia, myeloma, cytotoxic drug therapy and following gastrectomy, terminal ileum resection or disease

- Do not delay replacement therapy with folic acid and / or vitamin B12 by investigating the cause of the anaemia
- Ensure that vitamin B12 therapy is commenced with folic acid when both nutritional deficiencies exist, to avoid neurological complications.

Anaemia prior to scheduled major surgery whether mild or severe, is an independent risk factor for postoperative major morbidity and mortality. Major surgery should therefore be delayed until anaemia is corrected, if it is in the patient's best interests.

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MANAGEMENT OF THE ANAEMIC ADULT PATIENT PRIOR TO SCHEDULED MAJOR SURGERY

Aim:

To optimise haemoglobin and haemostasis prior to planned major surgery or other invasive procedures associated with blood loss

Objectives:

1. To ensure that all patients scheduled for major planned surgery are assessed for anaemia at least 4 – 6 weeks before the intended date of surgery
2. To ensure that anaemia is corrected promptly and appropriately before major surgery, when it is in the patient's best interests, even if this may result in delaying the date of surgery. Preoperative anaemia, whether mild or severe, is an independent risk factor for postoperative morbidity and mortality¹.
3. To ensure that the aetiology of anaemia is investigated and treated appropriately, provided it is in the patient's interests
4. To ensure that a patient's medication and intake of other substances, such as herbal remedies, is reviewed and adjusted as appropriate, to minimize the risk of perioperative bleeding.

Recommended plan of management:

1. Pre-assess a patient's medical and drug history at least 4-6 weeks before the intended date of surgery, when a full blood picture should be tested.
2. If a patient is found to be anaemic according to the WHO criteria² and the cause is not yet known, perform additional blood tests to determine whether the anaemia is due to iron, folate, vitamin B12 or other nutritional deficiency or to acute or chronic disease states, such as chronic kidney disease or inflammatory bowel disease (see the "4 STEPS IN THE INVESTIGATION AND MANAGEMENT OF THE ADULT PATIENT WITH ANAEMIA").
3. The cause of iron deficiency should always be investigated if not already known (see the "4 STEPS IN THE INVESTIGATION AND MANAGEMENT OF THE ADULT PATIENT WITH ANAEMIA").
4. Commence or continue iron or alternative replacement therapy as appropriate, without delay.
5. Aim to have the patient's haemoglobin in normal range (according to WHO criteria) before surgery. Surgery should be delayed to achieve this target, unless it is not in the patient's best interests.
6. Review a patient's medication and intake of other substances which could increase the risk of perioperative bleeding, e.g. herbal remedies. Consider the risks and benefits of continuing or discontinuing anti platelet and non steroidal anti-inflammatory drugs in the perioperative period.
7. Consider whether a patient on warfarin (or alternative anti thrombotic therapy) should be changed to prophylactic low dose low molecular weight heparin or higher dose bridging therapy – seek local guidance.

MANAGEMENT OF THE ANAEMIC ADULT PATIENT PRIOR TO SCHEDULED MAJOR SURGERY

(Also applicable to other invasive procedures with potential for blood loss)

WHO definition of anaemia²: adult male < 13g/dl; adult female < 12g/dl; pregnant female < 11g/dl

Pre assess patient at least 4 - 6 weeks before surgery
Assess medical and drug history
Test Full Blood Picture – if anaemic see below

Additional blood tests to determine type of anaemia

- Serum ferritin
- TIBC or TSAT
- Urea & electrolytes
- Liver function tests
- Serum folate and
- Vitamin B12 levels

Investigate cause of anaemia

- Refer to a clinical specialist (e.g. gastroenterologist) unless:
 - The cause has already been identified
 - or
 - It is not in the patient's best interests (e.g. palliative care patient)

Medication and other substances taken by patient

- Note which drugs and other substances (e.g. herbal remedies) could increase perioperative blood loss
- Advise patient to discontinue herbal remedies 2 weeks before surgery⁴

Follow 4 Steps algorithm for subsequent management of the adult patient with anaemia

Correct anaemia without delay

- Prescribe appropriate replacement therapy
- Monitor response to treatment after 3 weeks
- Continue or adjust therapy as appropriate
- Aim to have Hb in normal range before surgery³.
- Delay date of surgery, unless it is not in the patient's best interests

Treat the cause of anaemia

- Refer to appropriate clinical specialist for treatment as appropriate
- For newly detected anaemia it may be beneficial to fully evaluate the cause and associated clinical status before major surgery is undertaken²

Reduce perioperative blood loss

- Discontinue NSAIDs 24 hour preoperatively
- Consider risks vs benefits of preoperative discontinuation of anti platelet drugs (e.g. clopidogrel)
- Consider preoperative switch from warfarin to:
 - Low dose prophylactic LMWH
 - or
 - Bridging therapy with therapeutic LMWH (seek local guidance + expert advice)

TIBC = Total Iron Binding Capacity TSAT = transferrin saturation in %
NSAIDs = Non Steroidal Anti-inflammatory Drugs, e.g. Diclofenac, Ibuprofen
LMWH = Low Molecular Weight Heparin, e.g. Enoxaparin, Fondaparinux

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2. World Health Organisation. Worldwide Prevalence of Anaemia 1993-2005. WHO, 2008
3. Goodnough et al. Detection, evaluation, and management of preoperative anaemia in the elective orthopaedic surgical patient: NATA guidelines BJA 2011; 106: 13-22
4. Skinner CM and Rangasami. Preoperative use of herbal medicines: a patient survey J BJA 2002; 89: 792-5