Complete Summary

GUIDELINE TITLE

Guidelines on the management of acute myeloid leukaemia in adults.

BIBLIOGRAPHIC SOURCE(S)

British Committee for Standards in Haematology, Milligan DW, Grimwade D, Cullis JO, Bond L, Swirsky D, Craddock C, Kell J, Homewood J, Campbell K, McGinley S, Wheatley K, Jackson G. Guidelines on the management of acute myeloid leukaemia in adults. Br J Haematol 2006 Nov;135(4):450-74. [181 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

- Acute myeloid leukemia
- Acute promyelocytic leukemia
- Autologous or allogeneic stem cell transplantation
- Pregnancy

GUIDELINE CATEGORY

Diagnosis
Management

Risk Assessment
Treatment

CLINICAL SPECIALTY

Geriatrics
Hematology
Nursing
Obstetrics and Gynecology
Oncology
Pathology
Psychology
Radiology

INTENDED USERS

Advanced Practice Nurses
Clinical Laboratory Personnel
Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

To provide guidance to health care providers on the diagnosis and treatment of acute myeloid leukaemia and acute promyelocytic leukaemia

TARGET POPULATION

Adult patients, including pregnant women and the elderly, in the United Kingdom with acute myeloid leukaemia or acute promyelocytic leukaemia

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnosis/Prognosis Testing

1. Bone marrow aspirate and trephine biopsy
2. Morphological categorization
3. Immunophenotyping
4. Cytochemistry
5. Cytogenetics testing for using reverse transcription polymerase chain reaction and fluorescent in situ hybridization

Treatment/Management of Acute Myelogenous Leukemia (AML)

1. General measures and supportive case including rasburicase
2. Use of prophylactic antibiotics (not recommended for routine use)
3. Use of growth factors (not recommended for routine use)
4. Intensive chemotherapy (participation in National Cancer Research Institute Study [NCRI]) in patients able to tolerate it
5. Standard chemotherapy (daunorubicin and cytarabine)

6. Non-intensive chemotherapy (low-dose cytarabine)
7. Best supportive care (transfusion and hydroxycarbamide)
8. Management of AML in pregnancy
    - Avoidance of chemotherapy in first trimester
    - Consideration of early labor induction or termination
    - Use of all trans-retinoic acid (ATRA)
9. Management of extramedullary leukemia using systemic antileukemic chemotherapy
10. Management of AML in the elderly
    - Standard chemotherapy (e.g., daunorubicin + cytarabine
    - Non-intensive palliative treatment
    - Investigational treatment (e.g., gemtuzumab ozogamicin)

Treatment/Management of Acute Promyelocytic Leukemia (APL)

1. ATRA therapy as soon as diagnosis is suspected
2. Avoidance of leukopheresis
3. Treatment of coagulopathy to maintain platelet count (fresh frozen plasma, cryoprecipitate)
4. Dexamethasone for differentiation syndrome
5. Documentation of underlying PML-RARA fusion
6. Induction with ATRA plus anthracycline-based chemotherapy in PML-RARA-positive APL, followed by anthracycline-based consolidation therapy
7. Offer of entry into NCRI trial
8. Molecular monitoring to guide further therapy
9. Management of relapsed disease
    - Avoidance of single-agent ATRA
    - Use of arsenic trioxide (ATO) only in confirmed PML-RARA-positive APL
    - Treatment guided by minimal residual disease (MRD) assessment

Bone Marrow Transplantation (BMT) in AML

1. Patient education
2. Use of BMT only as salvage treatment
3. Preservation of fertility where possible
4. Allogenic transplantation based on risk assessment
5. Reduced-intensity conditioning allografts
6. Haplo-identical transplants
7. Autografting (in clinical trials only)

MAJOR OUTCOMES CONSIDERED

- Severe infection
- Antibiotic usage
- Duration of hospitalization
- Treatment side effects
- Complete remission rate
- Disease-free survival
- Overall survival

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The PubMed, Cochrane and Medline databases in the English language were searched using the key words 'acute myeloid leukaemia/leukemia', 'acute promyelocytic leukaemia/leukemia', 'stem cell transplantation' with subheadings 'anthracycline', 'pregnancy', 'disseminated intravascular coagulation' (DIC), 'growth factors' and 'quinolones' from 1983 to 2005.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Classification of Evidence Levels

Ia. Evidence obtained from meta-analysis of randomized controlled trials.

Ib. Evidence obtained from at least one randomised controlled trial.

IIa. Evidence obtained from at least one well-designed controlled study without randomisation.

IIb. Evidence obtained from at least one other type of well-designed quasi-experimental study.

III. Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

IV. Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

The authors have substantial experience in their field. Stakeholder involvement was secured through patient representation from the Leukaemia Research Fund and the Leukaemia Care Society. The recommendations were agreed using the Agree instrument (http://www.agreecollaboration.org).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Classification of Grades of Recommendations

Grade A. Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing specific recommendation (evidence levels Ia and Ib).

Grade B. Requires the availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (evidence levels IIa, IIb and III).

Grade C. Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (evidence level IV).

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The recommendations were reviewed by a Sounding Board of 100 haematologists representing adult practice in both teaching and district hospitals.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendation grades (**A-C**) and levels of evidence (**Ia-IV**) are defined at the end of the "Major Recommendations" field.

Key Recommendations

Diagnosis

1. Bone marrow aspirate and trephine biopsy unless the peripheral blast count is high.
2. Immunophenotyping [CD3, CD7, CD13, CD14, CD33, CD34, CD64, CD117 and cytoplasmic myeloperoxidase (MPO)].
3. Cytochemistry (MPO or Sudan Black, combined esterase). Can be omitted if four-colour flow cytometry is available.
4. Cytogenetics [with reverse-transcription polymerase chain reaction (RT-PCR) for AML 1-ETO and CBFB-MYH11 in non-acute promyelocytic leukaemia (APL) and promyelocytic leukaemia (PML) and retinoic acid receptor-alpha (RARA) in suspected APL; fluorescent in situ hybridisation (FISH) in selected cases].

Treatment

1. Patients should be treated by a multidisciplinary team that is experienced in the management of acute myeloid leukaemia (AML), serving a population base of 0.5 million and intensively treating five or more patients per annum (**recommendation grade C; evidence level IV**).
2. All eligible patients up to age 60 years (or older than 60 years but able to receive intensive treatment) with de novo or secondary AML should be asked to participate in the current National Cancer Research Institute (NCRI) study, at present AML 15 (http://www.aml15.bham.ac.uk) (**recommendation grade C; evidence level IV**).
3. Patients over 60 years old who are unable to tolerate remission induction chemotherapy, but are suitable for non-intensive therapy, should be asked to participate in the current NCRI study, at present AML 16 (http://www.aml16.bham.ac.uk) (**recommendation grade C; evidence level IV**).
4. Patients opting for non-intensive chemotherapy who are not entered into clinical trials should be offered treatment with low-dose cytarabine (**grade A; evidence level Ib**). Patients not able to tolerate chemotherapy should be given best supportive care: transfusion support and hydroxycarbamide to control the white cell count (**recommendation grade A; evidence level Ib**).

Acute Promyelocytic Leukaemia

1. All trans-retinoic acid (ATRA) should be started as soon as the diagnosis is suspected (**grade A; evidence level Ib**).
2. Leucopheresis should be avoided in patients a high white cell count (**grade B; evidence level III**).
3. The platelet count should be maintained at $>50 \times 10^9$ per liter, together with fresh frozen plasma (FFP) and cryoprecipitate to normalise the activated partial thromboplastin time and fibrinogen levels (**grade B; evidence level IIb**).

4. Differentiation syndrome should be treated promptly with dexamethasone 10 mg twice daily intravenous (iv), and ATRA stopped temporarily until the symptoms resolve (**grade C; evidence level IV**).
5. Diagnostic work-up should include documentation of underlying PML–RARA fusion (**grade B; evidence level IIa**).
6. Patients with PML–RARA-positive APL, deemed suitable for intensive therapy, should be treated with concurrent ATRA and anthracycline-based chemotherapy for induction, followed by anthracycline-based consolidation therapy (**grade A; evidence level 1b**).
7. Patients should undergo molecular monitoring after treatment to guide further therapy (**grade B; evidence level IIa**).
8. For relapsed disease, ATRA should not be used as single agent therapy due to the significant possibility of acquired secondary resistance and arsenic trioxide (ATO) should only be used in patients with confirmed PML–RARA-positive APL. Treatment of relapse, with respect to use of autologous or allogeneic transplantation as consolidation should be guided by minimal residual disease (MRD) assessment (**grade B; evidence level IIa**).

Pregnancy

1. AML in pregnancy should be managed jointly between the haematologist and the obstetrician with full involvement of the mother (**grade B; evidence level III**).
2. Chemotherapy in the first trimester is associated with a high risk of fetal malformation and should be avoided if possible. The opportunity to terminate the pregnancy should be discussed with the mother. If termination is refused and the mother's life is at risk, chemotherapy should be started (**grade B; evidence level III**).
3. Chemotherapy in the second and third trimesters is associated with an increased risk of abortion and premature delivery as well as low birth weight babies. Consideration should be given to early induction of labour between cycles of chemotherapy (**grade B; evidence level III**).

Transplantation

1. Allogeneic transplantation should be offered to patients with high-risk AML in first remission who have a human leucocyte antigen (HLA) identical donor, although it is accepted that only a minority of patients will benefit (**recommendation grade B; evidence level III**). Standard risk patients may be offered allo-transplantation as part of a clinical trial (**recommendation grade B; evidence level III**).
2. HLA-matched sibling allogeneic transplantation may be the treatment of choice for younger patients who are in second remission (**recommendation grade B; evidence level III**).
3. Older patients with high-risk disease or beyond first remission may be offered a reduced-intensity conditioned transplant but this should be in the context of a clinical trial (**recommendation grade C; evidence level IV**).
4. Younger high-risk patients or those beyond first remission may be considered for a haplo-identical transplant but this should be in the context of a clinical trial (**recommendation grade C; evidence level IV**).

5. The role of autografting in the management of AML is contentious. Autografting should only be carried out in a clinical trial (**recommendation grade A; evidence level Ia**).

Classification of AML

Minimum Laboratory Requirements for the Diagnosis of AML

1. Bone marrow aspirate and trephine biopsy unless the peripheral blast count is high.
2. Immunophenotyping (CD3, CD7, CD13, CD14, CD33, CD34, CD64, CD117, and cytoplasmic MPO) and HLA-DR.
3. Cytochemistry (MPO or Sudan Black, combined esterase). Can be omitted if four-colour flow is available.
4. Cytogenetics (with RT-PCR for *AML1-ETO* and *CBFB-MYH11* in non-APL and *PML-RARA* in suspected APL; FISH in selected cases).

Treatment of AML

General Measures and Supportive Care

1. Rasburicase should be used with chemotherapy in patients with hyperleucocytosis at risk of acute tumour lysis syndrome. (**recommendation grade B; evidence level IIb**).
2. There is no firm evidence of a survival advantage to support the routine use of prophylactic antibiotics in patients with AML and they are currently not recommended. (**recommendation grade B; evidence level IIb**)
3. There is no survival benefit from the use of growth factors following AML chemotherapy but growth factor use does reduce the duration of neutropenia, of antibiotic use and of hospital stay. The cost benefit advantages of routine growth factor use are uncertain. The routine use of growth factor therapy in AML is not recommended (**recommendation grade A; evidence level IIa**)

Treatment of Younger Adult Patients

1. All eligible patients up to the age of 60 years (or >60 years but able to receive intensive treatment) with *de novo* or secondary AML should be asked to participate in the current NCRI study, at present AML 15 (http://www.aml15.bham.ac.uk).
2. Patients over 60 years who are able to tolerate remission-induction chemotherapy should be asked to participate in the current NCRI study, at present LRF AML14 (http://www.aml14.bham.ac.uk) or HOVON/SAKK AML43.
3. Patients not eligible or unwilling to participate in the NCRI studies should be offered standard daunorubicin and cytarabine 3 + 10 or 3 + 7 induction chemotherapy (**Level 1b**).
4. Patients opting for non-intensive chemotherapy who are not entered into clinical trials should be offered treatment with low-dose cytarabine (**grade A; evidence level Ib**). Patients not able to tolerate chemotherapy should be given best supportive care: transfusion support and hydroxycarbamide to control the white count (**recommendation grade A; evidence level Ib**).

Management of AML in Patients Who Are Pregnant

1. AML in pregnancy should be managed jointly between the haematologist and the obstetrician with full involvement of the mother (**grade B; evidence level III**).
2. Chemotherapy in the first trimester is associated with a high risk of fetal malformation and should be avoided if possible. The opportunity to terminate the pregnancy should be discussed with the mother. If termination is refused and the mother's life is at risk, chemotherapy should be started (**grade B; evidence level III**)
3. Chemotherapy in the second and third trimesters is associated with an increased risk of abortion and premature delivery as well as low birth weight babies. Consideration should be given to early induction of labour between cycles of chemotherapy (**grade B; evidence level III**).
4. ATRA can be used in pregnancy in the second and third trimesters (**grade B; evidence level III**).

Management of Extramedullary Disease

1. Patients presenting with extramedullary leukaemia should receive systemic antileukaemic chemotherapy (**grade C; evidence level IV**).

<u>Acute Promyelocytic Leukaemia</u>

1. ATRA should be started as soon as the diagnosis is suspected (**grade A; evidence level Ib**).
2. Leucopheresis should be avoided in high count patients (**grade B; evidence level III**).
3. The coagulopathy should be treated to keep the platelets $>50 \times 10^9$/l, together with FFP and cryoprecipitate to normalize the activated partial thromboplastin time (APTT) and fibrinogen levels (**grade B; evidence level IIb**).
4. Differentiation syndrome should be treated promptly with dexamethasone 10 mg twice daily i.v., until the symptoms resolve (**grade C; evidence level IV**).
5. Diagnostic work-up should include documentation of underlying *PML-RARA* fusion (**grade B; evidence level IIa**).
6. Patients with PML-RARA positive APL, deemed suitable for intensive therapy, should be treated with concurrent ATRA and anthracycline-based chemotherapy for induction, followed by anthracycline-based consolidation therapy and should be offered entry into the NCRI AML trial (currently AML15) **(grade A; evidence level Ib**).
7. Patients should undergo molecular monitoring after treatment to guide further therapy (**grade B; evidence level IIa**).
8. For relapsed disease, ATRA should not be used as single agent therapy due to the significant possibility of acquired secondary resistance and ATO should only be used in patients with confirmed PML-RARA positive APL (**grade B; evidence level IIa**).Treatment of relapse, with respect to use of autologous or allogeneic transplantation as consolidation should be guided by minimal residual disease (MRD) assessment.

<u>Transplantation in AML</u>

1. Patients should be fully informed of both the advantages and disadvantages of the available treatments, and of the strategies that can be used to treat long-term side-effects, particularly in the area of sexual function and infertility.
2. Intensive consolidation chemotherapy treatment during first clinical remission should be offered as the preferred treatment to patients with favourable cytogenetics and to those unwilling to accept the risk of permanent damage to their sexual health and fertility, with bone marrow transplantation (BMT) remaining as the choice for salvage treatment in the event of relapse.
3. All patients of childbearing years undergoing BMT should be offered the opportunity of preserving their fertility (where possible) prior to treatment.
4. Allogeneic transplantation should be offered to patients with high-risk AML (risk groups are defined in Table II in the original guideline document) in first remission who have an HLA identical donor, although it is accepted that only a minority of patients will benefit (**recommendation grade B; evidence level III**). Standard risk patients may be offered allo-transplantation as part of a clinical trial (**recommendation grade B; evidence level III**).
5. Allogeneic transplantation may be the treatment of choice for younger patients who are in second remission (**recommendation grade B; evidence level III**).
6. Older patients with high-risk disease or beyond first remission may be offered a reduced intensity conditioned transplant but this should be in the context of a clinical trial (**recommendation grade C; evidence level IV**).
7. Younger high-risk patients or those beyond first remission may be considered for a haplo-identical transplant but this should be in the context of a clinical trial (**recommendation grade C; evidence level IV**).
8. The role of autografting in the management of AML is contentious. Autografting should only be carried out in the context of a clinical trial (**recommendation grade A; evidence level Ib**).

Acute Myeloid Leukaemia in the Elderly

1. For patients in whom intensive chemotherapy is deemed justified (e.g., age <70 years, good performance status, WBC $<100 \times 10^9$/l, no adverse cytogenetic abnormalities or MDR expression), standard induction chemotherapy with daunorubicin (or an equivalent anthracycline) for 3 days plus cytarabine for 7 to 10 days is recommended (**grade A recommendation, level Ib evidence**). Where possible patients should be entered into clinical trials.
2. There is no firm evidence to date to support the use of MDR-blocking agents as an adjunct to induction chemotherapy (**grade A recommendation, level Ib evidence**).
3. Similarly there is insufficient evidence to support routine use of granulocyte colony stimulating factor (G-CSF) or granulocyte-macrophage colony stimulating factor (GM-CSF) with induction chemotherapy in patients over 60 years of age, although this may be appropriate if it is desirable to reduce hospitalization or antibiotic usage (**grade A recommendation, level Ib evidence**).
4. The optimal postremission chemotherapy for older adult patients with AML remains unclear. There does not seem to be a role for extended consolidation chemotherapy or maintenance treatment (**grade A recommendation, level Ib evidence**).

5. Gemtuzumab ozogamicin shows promise as a salvage agent in patients with relapsed disease, and may be preferable to further intensive chemotherapy in this setting (**grade B recommendation, level IIb evidence**).

Non-Intensive (Palliative) Chemotherapy

1. Unless patients opting for palliative chemotherapy are entered into clinical trials, treatment should be offered with low-dose cytarabine (**grade A; level Ib evidence**).

Definitions:

Classification of Evidence Levels

Ia. Evidence obtained from meta-analysis of randomized controlled trials.

Ib. Evidence obtained from at least one randomised controlled trial.

IIa. Evidence obtained from at least one well-designed controlled study without randomisation.

IIb. Evidence obtained from at least one other type of well-designed quasi-experimental study.

III. Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

IV. Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

Classification of Grades of Recommendations

Grade A. Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing specific recommendation (evidence levels Ia and Ib).

Grade B. Requires the availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (evidence levels IIa, IIb and III).

Grade C. Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality (evidence level IV).

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Accurate diagnosis of acute myeloid leukaemia or promyelocytic leukaemia
- Accurate prognosis of the disease
- Appropriate treatment of the disease with improved overall and disease-free survival

POTENTIAL HARMS

Treatment of Acute Myeloid Leukemia

- Myelosuppression
- Coagulopathy
- Retinoic acid syndrome
- Acute tumor lysis syndrome with life-threatening hyperkalemia
- Iron overload and allergic reaction associated with rasburicase therapy
- Bacterial and fungal infection

Stem Cell Transplantation

- Graft-versus-host disease
- Increased morbidity and mortality
- Increased cost
- Decreased quality of life

Pregnancy

- Chemotherapy during the first trimester is teratogenic and associated with an increased risk of abortion and should be avoided if possible.
- If termination of pregnancy is unacceptable, this presents a considerable management dilemma as delay in treatment is associated with an adverse outcome and the risks of delay must be explained. Chemotherapy can proceed but is associated with increased risks of early fetal loss, congenital malformation and low birth weight.
- Chemotherapy given close to delivery may result in significant fetal pancytopenia requiring intensive support.

CONTRAINDICATIONS

CONTRAINDICATIONS

- Leukopheresis is contraindicated in patients with suspected acute promyelocytic leukaemia (APL), as it can exacerbate the coagulopathy with fatal consequences.
- Tranexamic acid may be useful for local bleeding, e.g., oral haemorrhage, but is contraindicated in the presence of haematuria because of the possibility of ureteric clot formation.
- Chemotherapy during the first trimester is teratogenic and associated with an increased risk of abortion and should be avoided if possible.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

While the advice and information in these guidelines is believed to be true and accurate at the time of going to press, neither the authors, nor the British Society for Haematology nor the publishers accept any legal responsibility for the content of these guidelines.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

End of Life Care
Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

British Committee for Standards in Haematology, Milligan DW, Grimwade D, Cullis JO, Bond L, Swirsky D, Craddock C, Kell J, Homewood J, Campbell K, McGinley S, Wheatley K, Jackson G. Guidelines on the management of acute myeloid leukaemia in adults. Br J Haematol 2006 Nov;135(4):450-74. [181 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Nov

GUIDELINE DEVELOPER(S)

British Committee for Standards in Haematology - Professional Association

SOURCE(S) OF FUNDING

British Committee for Standards in Haematology

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: DW Milligan; D Grimwade; JO Cullis; L Bond; D Swirsky; C Craddock; J Kell; J Homewood; K Campbell; S McGinley; K Wheatley; G Jackson

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

D Grimwade is supported by Leukaemia Research Fund of Great Britain and the European LeukemiaNet.

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the British Committee for Standards in Haematology Web site.

Print copies: Available from the British Committee for Standards in Haematology; Email: bcsh@b-s-h.org.uk.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on May 28, 2008. The information was verified by the guideline developer on June 30, 2008.

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