

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Neutropenic sepsis: prevention and management of neutropenic sepsis in cancer patients

1.1 *Short title*

Neutropenic sepsis

2 The remit

The Department of Health has asked NICE: 'To produce a clinical guideline on the prevention and management of neutropenic sepsis in cancer patients'.

3 Clinical need for the guideline

3.1 *Epidemiology*

- a) Neutropenic sepsis is a recognised and potentially fatal complication of anti-cancer treatment (particularly chemotherapy), although there are no accurate data available for morbidity and mortality in adults. For example, mortality rates have variously been reported as between 2 and 21%. Neutropenic sepsis is the second most common reason for hospital admission among children and young people with cancer, with approximately 4000 episodes occurring annually in the UK.
- b) The clinical endpoints of an episode of neutropenic fever can be described in descending order of adversity as: death, intensive care admission, medical complication (for example, need for supplemental oxygen, worsening renal function or hepatic

impairment), bacteremia (bacteria in the bloodstream), significant bacterial infection, or no adverse after effects.

- c) Adopting a policy of aggressive use of inpatient intravenous antibiotics in such episodes has reduced the mortality rate dramatically, for example in children and young adults from 30% in the 1970s to 1% in the late 1990s. Intensive care management is needed in less than 5% of cases.

3.2 Current practice

- a) Systemic therapies to treat cancer have a risk of reducing the bone marrow's ability to respond to infection by reducing its ability to produce a type of white blood cell known as a neutrophil. This is particularly the case with systemic chemotherapy, although radiotherapy may also cause such suppression. Neutropenic sepsis is the term used to describe a significant inflammatory response to a bacterial infection in a person with neutropenia (lack of neutrophils), with or without fever. Neutropenic fever refers to a clinical scenario in which a person with neutropenia presents with fever, with or without evidence of significant complications of infection. This is often also called febrile neutropenia.
- b) Most chemotherapy is given in a day-case or outpatient setting so episodes of fever in a potentially neutropenic person, and obvious sepsis, will predominantly present in the community. People receiving chemotherapy and their carers are informed of the risk of neutropenic sepsis and the warning signs and symptoms. Neutropenic sepsis is a medical emergency that requires immediate hospital investigation and treatment.

A recent National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report (Systemic Anti-Cancer Therapy: For better, for worse? 2008) and follow-up National Chemotherapy Advisory Group (NCAG) report (Chemotherapy Services in England: Ensuring quality and safety Last modified date:30 March

2010 Gateway reference:12208) highlighted problems with the management of neutropenic sepsis in adults receiving chemotherapy. These included inadequate management of neutropenic fever leading to avoidable deaths, and the need for systems for urgent assessment and trust-level policies for dealing with neutropenic fever. It also highlighted variation in the provision of information on treatment of side effects and access to a 24-hour telephone advice.

- c) There is national variation in use of risk stratification, and also in the use of oral or intravenous antibiotics and in- or outpatient management policies.
- d) Evidence-based recommendations on the prevention, identification and management of this life threatening complication of cancer treatment will improve outcomes.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

- a) Children, young people and adults with cancer (haematological and solid tumour malignancies) receiving anti-cancer treatment.
- b) No subgroups needing special consideration have been identified.

4.1.2 Groups that will not be covered

- a) Neutropenia or neutropenic sepsis not caused by anti-cancer treatment.

4.2 *Healthcare setting*

- a) All settings in which NHS care is received.

4.3 *Clinical management*

4.3.1 Key clinical issues that will be covered

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

- a) Signs and symptoms in people with suspected neutropenic sepsis in the community that necessitate referral to secondary care.
- b) Education and support for patients and carers on the identification of neutropenic sepsis.
- c) Emergency assessment in secondary care of a person with suspected neutropenic sepsis.
- d) Appropriate initial investigations of suspected infection in a neutropenic patient in secondary care:
 - Definition of neutropenia and fever.
 - Routine investigations (for example, chest radiography, urine culture, throat swabs, peripheral blood cultures).
- e) Risk stratification and management of suspected bacterial infection:
 - Clinically applied risk stratification scores or algorithms.
 - Inpatient versus ambulatory (non-hospitalised) management strategies.

- Oral antibiotic therapy, intravenous antibiotic monotherapy or intravenous antibiotic dual therapy.
 - Timing of initial antibiotic therapy.
 - Switching from intravenous to oral antibiotic therapy.
 - Management of unresponsive fever (excluding fungal infection).
 - Duration of empiric antibiotic therapy (antibiotic(s) chosen in the absence of an identified bacterium).
 - Duration of inpatient care.
- f) Primary and secondary prophylaxis in people at risk of neutropenic sepsis during anti-cancer treatment:
- Primary prophylaxis with growth factors (for example granulocyte colony stimulating factor) and/or antibiotics (for example fluoroquinolones).
 - Secondary prophylaxis with growth factors, granulocyte infusion and/or antibiotics.
- g) Role of empiric glycopeptide antibiotics (antibiotic(s) chosen in the absence of an identified bacterium) in patients with central lines and neutropenia or neutropenic sepsis.
- h) Indications for removing central lines in patients with neutropenia or neutropenic sepsis.
- i) Information and support for patients and carers that is. We think it is important that patient issues should be represented on the list of priority topics investigated by this guideline. What in your view are the information and support issues specific to patients with neutropenic sepsis and their carers or families.
- j) Training of all healthcare professionals on the identification and management of neutropenic sepsis.

4.3.2 Clinical issues that will not be covered

- a) Prophylaxis, investigation and management of non-bacterial infection.
- b) Investigation and management of graft versus host disease.
- c) Treatment of specific bacterial infections (for example bacterial pneumonia).
- d) Management of severe sepsis in intensive care units.
- e) Effect of neutropenic sepsis on subsequent chemotherapy scheduling and doses.
- f) Routine management of central lines and prevention of central line infection.

4.4 Main outcomes

- a) Mortality rate.
- b) Morbidity (for example renal impairment).
- c) Hospitalisation rates and length of hospital stay.
- d) Recurrence rate.
- e) Time to treatment of neutropenic sepsis.
- f) Health-related quality of life assessments (or surrogates, such as 'acceptability' or 'preference').

4.5 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually only be from an NHS and personal social services (PSS) perspective. Further

detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.6 Status

4.6.1 Scope

This is the consultation draft of the scope. The consultation dates are 7 June to 5 July 2010.

4.6.2 Timing

The development of the guideline recommendations will begin in September 2010.

5 Related NICE guidance

5.1 Published guidance

- Advanced breast cancer. NICE clinical guideline 81 (2009). Available from www.nice.org.uk/guidance/CG81
- Early and locally advanced breast cancer. NICE clinical guideline 80 (2009). Available from www.nice.org.uk/guidance/CG80
- Medicines adherence. NICE clinical guideline 76 (2009). Available from www.nice.org.uk/guidance/CG76
- Prostate cancer. NICE clinical guideline 58 (2008). Available from www.nice.org.uk/guidance/CG58
- Acutely ill patients in hospital. NICE clinical guideline 50 (2007). Available from www.nice.org.uk/guidance/CG50
- Improving outcomes for people with brain and other CNS tumours. NICE cancer service guidance (2006). Available from www.nice.org.uk/CSGBraincns
- Improving outcomes for people with sarcoma. NICE cancer service guidance (2006). Available from www.nice.org.uk/CSGSarcoma
- Improving outcomes for people with skin tumours including melanoma. NICE cancer service guidance (2006). Available from www.nice.org.uk/CSGSTIM

- Improving outcomes in children and young people with cancer. NICE cancer service guidance (2005). Available from www.nice.org.uk/CSGCYP
- Lung cancer. NICE clinical guideline 24 (2005). Available from www.nice.org.uk/guidance/CG24
- Improving outcomes in colorectal cancers. NICE cancer service guidance (2004). Available from www.nice.org.uk/CSGCC
- Improving outcomes in head and neck cancers. NICE cancer service guidance (2004). Available from www.nice.org.uk/CSGHN
- Improving outcomes in haematological cancers. NICE cancer service guidance (2003). Available from www.nice.org.uk/CSGHO
- Improving outcomes in breast cancer. NICE cancer service guidance (2002). Available from www.nice.org.uk/CSGBC
- Improving outcomes in urological cancers. NICE cancer service guidance (2002). Available from www.nice.org.uk/CSGUC

5.2 *Guidance under development*

NICE is currently developing the following related guidance (details available from the NICE website).

- Metastatic malignant disease of unknown primary origin. NICE clinical guideline. Publication expected July 2010.
- Lung cancer (update). NICE clinical guideline. Publication expected March 2011.
- Ovarian cancer. NICE clinical guideline. Publication expected April 2011.
- Colorectal cancer. NICE clinical guideline. Publication expected October 2011.

6 Further information

Information on the guideline development process is provided in:

- 'How NICE clinical guidelines are developed: an overview for stakeholders' the public and the NHS'
- 'The guidelines manual'.

These are available from the NICE website (www.nice.org.uk/GuidelinesManual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk).