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 consequences of an episode of infection in a neutropenic person 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. It may also lead to delay or modification of subsequent courses of chemotherapy.

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 Europe in the 1970s to 1% in the late 1990s. Intensive care management is needed in fewer than 5% of cases in England.

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.

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.

c) A report by the National Confidential Enquiry into Patient Outcome and Death report ('Systemic anti-cancer therapy: for better, for worse?', 2008) and a follow-up report by the National Chemotherapy Advisory Group ('Chemotherapy services in England: ensuring quality and safety', 2010) 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.

d) There is national variation in the use of:

- primary and secondary prophylaxis
- risk stratification in episodes of febrile neutropenia
- oral or intravenous antibiotics
- growth factors
- in- or outpatient management policies.

e) Evidence-based recommendations on the prevention, identification and management of this life threatening complication of cancer treatment are expected to 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. The guideline will define febrile neutropenia/neutropenic fever and neutropenic sepsis.

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/tertiary care.

b) Education and support for patients and carers on the identification of neutropenic sepsis.

c) Emergency assessment in secondary/tertiary 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.
- Investigations appropriate for risk stratification and management.

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.
- Duration of empiric antibiotic therapy (antibiotics 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 (antibiotics 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.

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 by intensive/critical 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 final scope.

4.6.2 Timing

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

5 Related NICE guidance

5.1 Published guidance

- Metastatic malignant disease of unknown primary origin (2010). NICE clinical guideline 104. Available from www.nice.org.uk/guidance/CG104
- 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 supportive and palliative care for adults with cancer. NICE cancer service guidance (2004). Available from www.nice.org.uk/CSGSP
- 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
- Improving outcomes in upper gastro intestinal cancers. Service guidance (2001). Available from www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4010025
- Improving outcomes in gynaecological cancers. Service guidance (1999). Available from www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4005385
- Improving outcomes in lung cancer. Service guidance (1998). Available from www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_4009184

5.2 Guidance under development

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

- 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).