**NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE**

# SCOPE

## 1 Guideline title

Diagnosis and management of metastatic malignant disease of unknown primary origin

### *1.1 Short title*

Metastatic malignant disease of unknown primary origin

## 2 Background

a) The National Institute for Health and Clinical Excellence ('NICE' or 'the Institute') has commissioned the National Collaborating Centre for Cancer to develop a clinical guideline on the diagnosis and management of metastatic malignant disease of unknown primary origin for use in the NHS in England and Wales. This follows referral of the topic by the Department of Health (see appendix). The guideline will provide recommendations for good practice that are based on the best available evidence of clinical and cost effectiveness.

b) The Institute's clinical guidelines support the implementation of National Service Frameworks (NSFs) in those aspects of care where a Framework has been published. The statements in each NSF reflect the evidence that was used at the time the Framework was prepared. The clinical guidelines and technology appraisals published by the Institute after an NSF has been issued have the effect of updating the Framework.

c) NICE clinical guidelines support the role of healthcare professionals in providing care in partnership with patients, taking account of their individual needs and preferences, and ensuring that patients (and

their carers and families, where appropriate) can make informed decisions about their care and treatment.

# 3 Clinical need for the guideline

a) Most patients with newly diagnosed cancer are found to have a clearly defined primary tumour after initial investigation and staging. However, a significant minority (about 5%) are eventually found to have metastatic malignancy without an identifiable primary site, despite exhaustive tests. On the basis of figures from the Office for National Statistics for 2000, at least 10,000 such cases occur annually in England and Wales. These 'unknown primary' cases pose additional problems to those encountered when a primary tumour is evident and where recognised management processes have been defined. These problems include:

- uncertainty about the nature, timing and extent of appropriate investigation
- over- or under-investigation
- failure to use valuable, effective treatments in certain cases (for example, in occult breast cancer or extra-gonadal germ cell tumour)
- inappropriate use of some expensive palliative treatments of limited or uncertain value
- unstructured use of potentially valuable but costly new technologies such as positron emission tomography (PET) scanning, genetic profiling and targeted therapies
- inadequate reporting of data such as incidence and waiting time
- poor patient access to cancer information and support facilities
- the absence of a structured research programme.

b) There are no national clinical guidelines on this topic currently being developed in the UK. Neither the NICE guideline ‘Referral guidelines for suspected cancer’ (NICE clinical guideline 27) nor

any of the NICE cancer service guidance addresses the needs of this group of patients.

c) Most patients with cancer currently benefit from a multidisciplinary approach to management of their disease, based on agreed local guidelines for investigation and treatment. One quite large subset of patients is those who present with metastatic cancer without an identified primary site. However, the heterogeneous nature of patients with an undiagnosed primary cancer and their varied clinical problems mean that current management is likely to be very variable and inefficient. Therefore, specifically designed guidelines would improve the management of this group of patients.

d) The aim of this guideline is to clarify the investigation of patients with metastatic malignancy disease from an undiagnosed primary cancer and to define optimal treatment for patients who eventually have no primary cancer identified.

# 4 The guideline

a) The guideline development process is described in detail in two publications that are available from the NICE website (see ‘Further information’). ‘The guideline development process: an overview for stakeholders, the public and the NHS’ describes how organisations can become involved in the development of a guideline. ‘The guidelines manual’ provides advice on the technical aspects of guideline development.

b) This document is the scope. It defines exactly what this 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 (see appendix).

c) 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) Adults (18 years and older) who have a provisional diagnosis of metastatic malignant disease with or without histological or cytological confirmation, in whom a primary site has not been identified and in whom further investigation is needed.

b) Adults who, following appropriate investigation, are found to have histologically or cytologically confirmed metastatic carcinoma but no apparent site of primary tumour, and for whom subsequent management needs to be considered.

c) Adults who have had a previous diagnosis of cancer treated with a curative intent, who present with metastatic malignant disease and in whom it is uncertain whether this is a recurrence or related to a new primary tumour.

### 4.1.2 Groups that will not be covered

a) Children (younger than 18) with metastatic malignant disease of unknown primary site.

b) Adults with histologically or cytologically confirmed malignant lymphoma.

c) Adults with histologically or cytologically confirmed metastatic carcinoma or sarcoma in whom the primary site of tumour is established or highly probable.

d) Adults with no histological or cytological confirmation of metastatic malignant disease but with an established or highly probable primary site on the basis of clinical examination or imaging.

## *4.2 Healthcare setting*

a) Primary care.

b) Secondary care, including all departments and specialties where these patients may present and be managed, such as general acute medicine (and its subspecialties); general surgery; orthopaedic surgery; ear, nose and throat surgery; gynaecology and care of the elderly.

c) Tertiary care in cancer centres and regional specialties such as neurosurgery and plastic surgery.

## *4.3 Clinical management*

a) Diagnosing the primary site of metastatic malignant disease using:

- histological, cytological and molecular techniques
- imaging techniques
- invasive operative techniques (such as image-guided biopsy or laparoscopy)
- biochemical tests (such as 'tumour markers').

b) How investigations are best sequenced and organised to reach the most rapid diagnosis.

c) Which groups of patients are unlikely to benefit from extensive investigation.

d) What systemic therapy, if any, is effective in treating patients who, following appropriate investigation, are found to have histologically or cytologically confirmed metastatic carcinoma but no apparent site of primary tumour. Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only where 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 their decisions for individual patients.

e) The Guideline Development Group will consider making recommendations on the principal complementary and alternative interventions or approaches to care relevant to the guideline topic.

f) The Guideline Development Group will take reasonable steps to identify ineffective interventions and approaches to care. If robust and credible recommendations for re-positioning the intervention for optimal use, or changing the approach to care to make more efficient use of resources, can be made, they will be clearly stated. If the resources released are substantial, consideration will be given to listing such recommendations in the 'Key priorities for implementation' section of the guideline.

## *4.4 Status*

### 4.4.1 Scope

This is the consultation draft of the scope. The consultation period is 21 January until 18 February 2008.

### 4.4.2 Guideline

The development of the guideline recommendations will begin in May 2008.

# 5 Further information

Information on the guideline development process is provided in:

- 'The guideline development process: an overview for stakeholders, the public and the NHS'
- 'The guidelines manual'.

These booklets are available as PDF files from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the website.

# Appendix: Referral from the Department of Health

The Department of Health asked the Institute:

to prepare a clinical guideline on the diagnosis and management of metastatic malignant disease of unknown primary origin.