NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Diagnostics Assessment Programme

Fluorouracil plasma monitoring: the My5-FU assay for guiding dose adjustment in patients receiving fluorouracil chemotherapy by continuous infusion

Final scope

December 2013

1 Introduction

The My5-FU assay is manufactured by Saladax Biomedical Inc. The Medical Technologies Advisory Committee identified the My5-FU assay as potentially suitable for evaluation by the Diagnostics Assessment Programme on the basis of a briefing note. The final scope was informed by the assessment subgroup meeting held on 5th December 2013. A glossary of terms and a list of abbreviations are provided in appendices A and B.

2 Description of the technology

This section describes the properties of the diagnostic technology based on information provided to NICE from the manufacturer and on information available in the public domain. NICE has not carried out an independent evaluation of this description.

2.1 Purpose of the medical technology

The My5-FU assay (previously known as OnDose) is a CE-marked in vitro diagnostic test designed to measure the levels of fluorouracil (5-FU) chemotherapy in plasma samples. It is intended for use in patients who are receiving 5-FU chemotherapy by continuous infusion, to facilitate pharmacokinetic dose adjustment and therapeutic drug monitoring with the aim of achieving an optimal plasma level of the drug. 5-FU is amenable to therapeutic drug monitoring because it has a narrow therapeutic index, with doses below the therapeutic window potentially reducing treatment efficacy and doses above the window being more likely to cause side effects and toxicity. Commonly reported side effects of 5-FU chemotherapy include diarrhoea, oral and gastrointestinal mucositis, anaemia, fatigue, nausea and vomiting and palmar-plantar erythrodysesthesia (hand-foot syndrome), all of

which when severe can indicate the need to limit the dose. The consequences of 5-FU toxicity can include neuropathy (damage to nerve cells), severe damage to organs, cardiotoxicity, neutropenia, sepsis and septic shock (Hale et al, 2002). In addition, people with dihydropyrimidine dehydrogenase deficiency (DPD deficiency) have a reduced ability to metabolise 5-FU and can develop serious toxicity following treatment with 5-FU.

2.2 Product properties

The My5-FU assay is a homogenous two-reagent nanoparticle agglutination assay that can be adapted for use on a range of clinical chemistry analysers. It is based upon the measurement of changes in scattered light which is dependent on the level of agglutination of nanoparticles; agglutination is partially inhibited when 5-FU is present in the sample and results in less scattering of light. The assay requires a peripheral venous blood sample (not from the infusion port) which is taken towards the end of each 5-FU infusion cycle using an EDTA or heparin tube. Turnaround time is dependent on the analyser used but is around 10–15 minutes to the first result, with subsequent results following in less than a minute.

Results are reported in nanograms 5-FU/millilitre and are converted to an area under the curve (AUC) value in the laboratory, by multiplying the concentration of 5-FU in a steady state by the time of the infusion (in hours). This is then compared with a pre-defined optimal therapeutic range and the results, reported as mg·h/L, are used to guide the dose of 5-FU given in subsequent chemotherapy cycles. It is advised that AUC values of greater than 50 mg·h/L should be disregarded as this may signify that the blood sample has been taken too close to the infusion port. The assay has a limit of detection of 52 nanograms/millilitre and a lower limit of quantitation of 85 nanograms/millilitre. The My5-FU assay has been validated against liquid chromatography mass spectrometry (Beumer et al, 2009) and high performance liquid chromatography, laboratory techniques commonly used in pharmacokinetic studies.

When using the My5-FU assay in clinical practice, the initial dose of 5-FU is calculated according to a patient's body surface area and a sample of the patient's blood is taken towards the end of the infusion cycle, at least 18 hours after the start of the infusion. For example, during a 46 hour infusion it is recommended that a blood sample is taken 24 hours after the start of the infusion (with a sample collection window between hours 18 and 44), whilst the pump is infusing at a steady rate. The sample is stabilised and then sent to the hospital laboratory for analysis, with the results made available to clinicians in advance of the next chemotherapy cycle. Subsequent doses of 5-

FU are then calculated using the AUC result from the My5-FU assay, in accordance with a pre-determined dose adjustment algorithm. A published dose adjustment algorithm for patients with colorectal cancer (Kaldate et al, 2012) recommends an optimal therapeutic range of 20–30 mg·h/L with adjustments of no more than 30% of the dose for each infusion (see table 1). Patients typically require 3–4 adjustments to reach an optimal therapeutic range. Once the optimal range is achieved, or if the patient's 5-FU plasma level is already within the optimal range, the dose is maintained and plasma levels are retested at every 6th infusion cycle to ensure sustained optimal drug levels.

Table 1: 5-FU dose adjustment algorithm for colorectal cancer patients

AUC from previous cycle (mg·h/L)	Change in Dose (mg/m^2)
≥40	↓ 30%
37-39	↓ 25%
34-36	↓ 20%
31-33	↓ 10%
20-30	NO CHANGE NEEDED
17-19	↑ 10%
14-16	↑ 20%
8-13	↑ 25%
<8	Repeat previous dose, to eliminate chance of test error If AUC of <8 is repeated, then increase dose by ↑ 30%

Source: Kaldate et al. (2012)

3 Target conditions / indications

Fluoropyrimidine-based chemotherapy is used in the treatment of many different cancers. It can be administered as an infusion, as an injection, or orally (capecitabine). Fluoropyrimidine-based chemotherapy that is given as an infusion or an injection is known as 5-FU, which can be prescribed as either a single agent or in conjunction with other chemotherapy drugs, known as a regimen. A summary of some of the most commonly used 5-FU infusion chemotherapy regimens is given in Table 1.

Table 2: Examples of 5-FU infusion chemotherapy regimens

Regimen	Agents			
De Gramont	5-FU	folinic acid		
FOLFIRI	5-FU	folinic acid	irinotecan	
FOLFOXIRI	5-FU	folinic acid	oxaliplatin	irinotecan
FOLFOX	5-FU	folinic acid	oxaliplatin	
ECF	5-FU	epirubicin	cisplatin	

Chemotherapy is usually given as a course of treatments over 3-6 months. An average course of chemotherapy typically includes between 4-8 cycles, with each cycle including both the time when the chemotherapy is administered and a break to allow for recovery before the next administration of chemotherapy. Continuous infusions of 5-FU typically last for around 22-48 hours and usually require the patient to have a central venous access device such as a central line or PICC line. Some patients are able to have their 5-FU infusion via a portable pump which can enable them to go home during treatment.

Current NHS practice for calculating the dose of 5-FU a patient will receive is body surface area (BSA) dosing. BSA is calculated by formulae which use the patient's height and weight (see Appendix A), and is said to correlate with blood volume, cardiac output and renal function, all of which influence drug elimination (Drug and Therapeutics Bulletin, 2010). Usually the dose is calculated in accordance with the patient's actual bodyweight unless obesity, oedema or some other form of abnormal fluid retention such as ascites is present. In this case, ideal weight is used as the basis for the calculation (Drug and Therapeutics Bulletin, 2010). The dose may be adjusted to take into account a patient's liver and kidney function, both of which may impact upon how 5-FU is metabolised and excreted. A 5-FU dose may also be adjusted according to the severity of any side effects that a patient may be experiencing.

5-FU is commonly given to people with: colorectal cancer, head and neck cancer, stomach cancer, and pancreatic cancer. The treatment pathways for each disease are summarised below.

3.1 Colorectal cancer

3.1.1 Background

Colorectal cancer is the fourth most common cancer in the UK with around 40,000 new cases registered each year (CRUK CancerStats, 2013a). This represents 11% of all new cancer cases in women and 14% of all new cancer

cases in men (CRUK CancerStats, 2013a). Colorectal cancer accounts for 10% of all cancer deaths. In 2010, there were 15,708 deaths from bowel cancer in the UK (CRUK CancerStats, 2013b). Two-thirds of bowel cancers develop in the colon with the remaining third developing in the rectum. Around half of people diagnosed with colorectal cancer survive for at least five years after diagnosis (CRUK CancerStats, 2012a).

3.1.2 Care pathway

The care pathway for people with colorectal cancer is outlined in NICE Clinical Guideline 131 (CG131) Colorectal cancer: The diagnosis and management of colorectal cancer (2011).

Early stage colorectal cancer: Following tumour resection, adjuvant chemotherapy may be considered for people with high-risk stage II colon cancer, and most people with stage III colorectal cancer will be advised to have adjuvant therapy. The following are recommended as options for the adjuvant treatment of patients with stage III colon cancer:

- Capecitabine monotherapy
- Oxaliplatin in combination with 5-FU and folinic acid

The choice of adjuvant treatment is to be decided jointly by the patient and their clinician, taking into account contraindications and the side effect profile of the drugs, and the method of administration as well as the clinical condition and preferences of the individual. Neoadjuvant chemoradiation may also be recommended for people who are likely to have resectable tumours.

Treating advanced colorectal cancer: The chemotherapy drugs most frequently used in the treatment of advanced colorectal cancer are 5-FU, Capecitabine, Raltitrexed, Irinotecan, and Oxaliplatin. NICE CG131 makes the following recommendations on the treatment of metastatic colorectal cancer: “When offering multiple chemotherapy drugs to patients with advanced and metastatic colorectal cancer, consider one of the following sequences of chemotherapy unless they are contraindicated:

- FOLFOX (folinic acid plus fluorouracil plus oxaliplatin) as first-line treatment then single agent irinotecan as second-line treatment or;
- FOLFOX as first-line treatment then FOLFIRI (folinic acid plus fluorouracil plus irinotecan) as second-line treatment or;

- XELOX (capecitabine plus oxaliplatin) as first-line treatment then FOLFIRI (folinic acid plus fluorouracil plus irinotecan) as second-line treatment."

Raltitrexed may considered as an alternative for patients who are intolerant to 5-FU and folinic acid or for whom these drugs are not suitable, for example patients who develop cardiotoxicity.

Oral therapy with fluoropyrimidines is recommended as an option for first line treatment of metastatic colorectal cancer. NICE technology appraisal 61 (TA61) recommends both capecitabine and tegafur with uracil, as alternatives to intravenous 5-FU. When making a choice between oral and intravenous fluoropyrimidines clinicians should take into account contraindications and side effect profiles, the clinical condition and patient preferences. NICE Technology Appraisal 176 (TA176) also recommends cetuximab in combination with FOLFOX or FOLFIRI chemotherapy for the first line treatment of metastatic colorectal cancer in people with KRAS wild-type tumours in whom:

- The primary tumour has been resected or is potentially operable.
- The metastatic disease is confined to the liver and is unresectable
- The patient is fit enough to undergo surgery to resect the primary colorectal tumour and to undergo liver surgery if the metastases become resectable after treatment with cetuximab.

3.2 Head and neck cancer

3.2.1 Background

Head and neck cancer describes a variety of malignant tumours occurring in the head and neck region, mainly in the mouth and throat. Around 16,000 people in the UK are diagnosed with a head and neck cancer each year (NHS Choices, 2012). The average national incidence rates are 0.39 per 100,000 for nasopharyngeal cancer, 3.01 per 100,000 for laryngeal cancer and 3.02 per 100,000 for oral cancer (Oxford Cancer Intelligence Unit, 2010). Five year survival rates vary depending on the type of cancer; Thyroid cancer has an estimated five year survival rate of 87%, whereas the five year survival rate for Hypopharyngeal cancer is 26% (Oxford Cancer Intelligence Unit, 2010).

3.2.2 Care pathway

Localised head and neck cancers which have not spread to nearby lymph nodes are usually treated with surgery or radiotherapy, whilst cancers which are locally advanced and have spread to nearby lymph nodes are usually treated with chemotherapy and/or radiotherapy. Chemotherapy drugs which may be used to treat head and neck cancers include carboplatin, docetaxel, gemcitabine and 5-FU. The chemotherapy drugs prescribed vary depending on the location of the cancer:

- Nasal and sinus cancer: cisplatin, 5-FU, carboplatin, docetaxel, paclitaxel and gemcitabine.
- Nasopharyngeal cancer: cisplatin, 5-FU, docetaxel, paclitaxel and gemcitabine.
- Mouth and oropharyngeal cancer: cisplatin, 5-FU, carboplatin, bleomycin, methotrexate and docetaxel.
- Laryngeal cancer: cisplatin, 5-FU, carboplatin, taxol, capecitabine, and gemcitabine.
- Oesophageal cancer: epirubicin, 5-FU, capecitabine, cisplatin, oxaliplatin, taxol, irinotecan and vinorelbine.
- Salivary gland cancer: cisplatin, carboplatin, cyclophosphamide, doxorubicin, methotrexate and paclitaxel.

For people in whom platinum-based chemotherapy is contraindicated, NICE Technology Appraisal 145 (TA 145) Cetuximab for the treatment of locally advanced squamous cell cancer of the head and neck (2008) makes the following recommendation: “Cetuximab in combination with radiotherapy is recommended as a treatment option only for patients with locally advanced squamous cell cancer of the head and neck whose Karnofsky performance status score is 90% or greater and for whom all forms of platinum-based chemotherapy treatment are contraindicated”.

3.3 Stomach cancer

3.3.1 Background

Stomach cancer is the ninth most common cancer in males in the UK and fourteenth in females. The majority of cases are adenocarcinomas. There were 7,610 new cases of stomach cancer diagnosed in 2008 (CRUK

CancerStats, 2013c). Around 42% of people will survive for a year after diagnosis, although this falls to around 18% after 5 years (CRUK CancerStats, 2012b).

3.3.2 Care pathway

Treating early stage stomach cancer: Early stage stomach cancer is usually treated with surgery, with neo-adjuvant or adjuvant chemotherapy being offered where appropriate. Chemotherapy drugs used in the treatment of stomach cancer include cisplatin, epirubicin and 5-FU.

Treating advanced stomach cancer: Advanced stomach cancer is treated with chemotherapy. NICE Technology Appraisal 191 (TA191) capecitabine for the treatment of advanced gastric cancer (2010) recommends capecitabine in conjunction with a platinum-based regimen for the treatment of inoperable advanced gastric cancer. Capecitabine and platinum based regimens include epirubicin, cisplatin and capecitabine (ECX), epirubicin, oxaliplatin and capecitabine (EOX) and capecitabine and cisplatin (CX). 5-FU remains an alternative for people in whom capecitabine is contraindicated or otherwise unsuitable. This may include patients who are unable to tolerate oral administration, due to difficulty swallowing or nausea. NICE Technology Appraisal 208 (TA208) HER2 positive gastric cancer tratuzumab (2010) recommends trastuzumab in combination with cisplatin and capecitabine or 5-FU as an option for the treatment of HER2 positive metastatic adenocarcinoma of the stomach or gastro-oesophageal junction in people who have not received prior treatment for their metastatic disease and have tumours expressing high levels of HER2.

3.4 Pancreatic cancer

3.4.1 Background

Around 8,500 people were diagnosed with pancreatic cancer in the UK in 2010. It is the tenth most common cancer in the UK and the fifth most common cause of death from cancer, accounting for 2.6% of cancer cases and 5% of all cancer deaths (CRUK CancerStats, 2013d). Pancreatic cancer has a poor survival rate due to typical late presentation and early metastases. Less than a fifth of patients present with potentially curable tumours and the overall five-year survival rate is less than 5% (CRUK CancerStats, 2012c).

3.4.2 Care pathway

Chemotherapy drugs that may be used to treat pancreatic cancer are 5-FU, capecitabine, and gemcitabine. If surgery is possible, adjuvant treatment with 5-FU can reduce the risk of recurrence. Gemcitabine may also be used as it has a lower side effect profile than 5-FU.

NICE Technology Appraisal 25 (TA 25) Guidance in the use of gemcitabine for the treatment of pancreatic cancer (2001) recommends that gemcitabine may be considered as a treatment option for patients with advanced or metastatic adenocarcinoma of the pancreas and a Karnofsky performance score of 50 or more, where first line chemotherapy is to be used. Gemcitabine is not recommended for patients who are suitable for potentially curative surgery, or patients with a Karnofsky performance score of less than 50. The guidance also states that there was insufficient evidence to support the use of gemcitabine as a second line treatment in patients with pancreatic adenocarcinoma.

3.5 Patient issues and preferences

As fluoropyrimidine-based chemotherapy can be administered either orally or intravenously a joint decision is made between the clinician and the patient, taking into account the clinical situation and the patient's preference over the mode of administration. Although capecitabine does not require central venous access, the ability to reduce toxicity and improve the efficacy of treatment through monitoring and adjusting the dose of 5-FU administered by infusion may be an important consideration for patients.

4 Scope of the evaluation

Table 3: Scope of the evaluation

Decision question	What is the clinical and cost effectiveness of the My-5FU assay for the pharmacokinetic dose adjustment of continuous infusion 5-FU chemotherapy?
Populations	People receiving 5-FU chemotherapy by continuous infusion. If evidence permits, this will include people with: • Colorectal cancer • Head and neck cancer • Stomach cancer • Pancreatic cancer The use of My5-FU in patients receiving treatment in the adjuvant or metastatic setting should be considered separately if evidence permits. Population subgroups, in whom the use of the My5-FU assay may be particularly clinically and cost effective, should be considered separately if clinical outcomes allow. Such subgroups include: • People with DPD deficiency • People with impaired renal function • People with impaired liver function • People whose body surface area is outside the standard range for dosing 5-FU • People with a less favourable performance status who may be undertreated in current practice
Intervention	My5-FU assay
Comparator	Current clinical practice for calculating and adjusting the dose of 5-FU is body surface area dose adjustment Although not a comparator, high performance liquid chromatography and liquid chromatography-mass spectrometry should be considered the gold standard for the purpose of assessing the accuracy of 5-FU plasma level measurements
Healthcare setting	Oncology services in secondary or tertiary care settings. Continuous infusion 5-FU can be delivered through oncology outpatient services, with patients returning home once an infusion has begun.
Outcomes	Intermediate measures for consideration may include: • Proportion of patients with 5-FU plasma levels in

	the optimal target range • Area under the curve measurements • Incidence of over and under dosing • Frequency of dose adjustment • Test failure rates
	Clinical outcomes for consideration may include: • Treatment response rates • Progression free survival • Overall survival • Health related quality of life • Incidence of side effects and 5-FU toxicity
	Costs will be considered from an NHS and Personal Social Services perspective. Costs for consideration may include: • Cost of My5-FU testing • Cost of delivering 5-FU by infusion • Cost of side effects and 5-FU toxicity and their associated treatment or hospitalisation costs • Additional costs associated with changes to continuous infusion protocols.
	The cost-effectiveness of interventions should be expressed in terms of incremental cost per quality-adjusted life year.
Time horizon	The time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.

5 Modelling approach

5.1 Existing models

One study was identified during scoping, which reports the cost-effectiveness of pharmacokinetic dosing of 5-FU in people with metastatic colorectal cancer in the UK (Becker et al, 2013). A decision tree model taking the perspective of the NHS was used to estimate the lifetime cost-effectiveness of pharmacokinetic dose adjustment compared with body surface area dosing for commonly administered 5-FU infusion regimens. The model also includes treatment options which include bevacizumab, however this is not currently recommended by NICE for the treatment of metastatic colorectal cancer.

5.2 Modelling possibilities

It is likely that a linked evidence approach will be needed for the cost-effectiveness modelling. During scoping no end-to-end studies of the My5-FU assay were identified. Published evidence was found relating to: the validation of the My5-FU assay with LC-MS, the impact of 5-FU plasma levels on toxicity, pharmacokinetic variability of 5-FU when BSA dosing is used, and the impact of pharmacokinetic dose adjustment of 5-FU on survival. The available evidence can be linked and the cost-effectiveness of the My5-FU assay investigated through modelling and sensitivity analyses.

6 Equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

All people with cancer are covered by the disability provision of the equality act from the point of diagnosis. People who may be at greatest risk of 5-FU toxicity include people with impaired liver function, people with impaired renal function, people whose body surface area is outside the standard range for dosing 5-FU, and those who have a less favourable performance status (including older people) prior to commencing chemotherapy. These groups of people may gain the greatest benefit from reduced 5-FU toxicity, which may enable them to have treatment that may not otherwise be suitable for them. My5-FU may also be of particular benefit to people who are receiving 5-FU by continuous infusion for the treatment of metastatic disease, in whom a greater emphasis is placed on maintaining quality of life.

7 Implementation issues

Use of the My5-FU assay may require changes to local protocols to ensure that blood samples are taken towards of the end of the 5-FU infusion, and results are available to guide dose adjustment when the next chemotherapy cycle begins. There may also be an increased requirement for services to deliver 5-FU as an infusion, particularly for patients who would otherwise have opted to receive capecitabine.

Appendix A Glossary of terms

Area under the plasma drug concentration-time curve: the curve shows the plot of the plasma concentration level (mg/L) against time (hours [h]). The area under the curve represents the body's actual exposure to the drug after drug has been administered and is dependent upon both the dose administered and the rate of elimination of the drug from the body. Results of area under the drug concentration time curve are expressed in mg·h/L. Using the area under the plasma concentration-time curve to adjust drug dosing is a method of pharmacokinetic dose adjustment.

Body surface area dosing: a method of calculating the dose of a drug using body surface area in m^2. Body surface area (BSA) is calculated by formulae using the patient's height and weight. BSA is said to correlate with blood volume, cardiac output and renal function which influence drug elimination, but does not take into account other important factors such as coexisting illness, genetic variations, nutritional status, renal and hepatic function and previous response to chemotherapy (Drug and Therapeutics Bulletin, 2010).

Performance status: performance status is used to assess a person's general health, and may be used to determine whether a course of treatment is appropriate. Two commonly used scales for assessing performance status are the World Health Organisation (WHO) performance scale and the Karnofsky performance status scale. The scales differ, but both range from fully active with no evidence of disease to very ill with a high level of care required.

Pharmacokinetics: the study of the actions of the body on a drug and their impact on drug uptake rates. Considerations in pharmacokinetics include the mechanisms of drug absorption, distribution, metabolism and excretion.

Side effects: Side effects of chemotherapy are commonly graded according to systems such as the National Cancer Institute's Common Terminology for Adverse Events system, with grade one side effects being mild and grade five representing toxicity resulting in death.

Therapeutic range: the range from the lowest dose to the maximum tolerated dose.

Appendix B Abbreviations

BSA	Body surface area
5-FU	Fluorouracil
DHD	Dihydropyrimdine dehydrogenase
EDTA	Ethylenediaminetetraacetic acid (anticoagulant)
HPLC	High performance liquid chromatography
ICER	Incremental cost-effectiveness ratio
LC-MS	Liquid chromatography mass spectrometry
QALY	Quality adjusted life year

Appendix C Related NICE guidance and pathways

Related NICE guidance

Published guidance

Neutropenic sepsis: prevention and management of neutropenic sepsis in cancer patients. NICE Clinical Guidelines, CG151, September 2012. Available from http://guidance.nice.org.uk/CG151

Colorectal cancer. NICE Quality Standards, QS20, August 2012. Available from: http://www.nice.org.uk/guidance/QS20

Cetuximab, bevacizumab and panitumumab for the treatment of metastatic colorectal cancer after first-line chemotherapy: Cetuximab (monotherapy or combination chemotherapy), bevacizumab (in combination with non-oxaliplatin chemotherapy) and panitumumab (monotherapy) for the treatment of metastatic colorectal cancer after first-line chemotherapy. NICE Technology Appraisals, TA242, January 2012. Available from: http://guidance.nice.org.uk/TA242

Colorectal cancer: the diagnosis and management of colorectal cancer. NICE Clinical Guidelines, CG131, November 2011. Available from: http://www.nice.org.uk/guidance/CG131

Bevacizumab in combination with oxaliplatin and either fluorouracil plus folinic acid or capecitabine for the treatment of metastatic colorectal cancer. NICE Technology Appraisals, TA212, December 2010. Available from: http://www.nice.org.uk/guidance/TA212

Capecitabine for the treatment of advanced gastric cancer. NICE Technology Appraisals, TA191, July 2010. Available from: http://www.nice.org.uk/guidance/TA191

Cetuximab for the first line treatment of metastatic colorectal cancer. NICE Technology Appraisals, TA176, August 2009. Available from: http://www.nice.org.uk/guidance/TA176

Cetuximab for the treatment of metastatic and/or recurrent squamous cell carcinoma of the head and neck. NICE Technology Appraisals, TA172. June 2009. Available from: http://www.nice.org.uk/guidance/TA172

Cetuximab for the treatment of head and neck cancer. NICE Technology Appraisals, TA145, June 2008. Available from: http://www.nice.org.uk/guidance/TA145

Laparoscopic surgery for the treatment of colorectal cancer. NICE Technology Appraisals, TA105. August 2006. Available from: http://www.nice.org.uk/guidance/TA105

Improving outcomes in head and neck cancers. NICE Cancer service guidance CSGHN, November 2004. Available from: http://guidance.nice.org.uk/CSGHN

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Capecitabine and tegafur uracil for metastatic colorectal cancer. NICE Technology Appraisals, TA61, May 2003. Available from: http://www.nice.org.uk/guidance/TA61

Guidance in development

KRAS mutation testing of tumours in adults with metastatic colorectal cancer. NICE Diagnostics Assessment Programme. Publication expected: TBC. http://guidance.nice.org.uk/DT/14

Assessment and management of upper airways tract cancers. NICE clinical guideline. Publication expected: September 2015. http://guidance.nice.org.uk/CG/Wave0/668

Related pathways

The My5-FU guidance will be included in several NICE pathways, for example colorectal cancer

In this pathway, it may be appropriate to include the full recommendations of the guidance, in others it will only be necessary to give a link to the guidance.

Appendix D References

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CRUK CancerStats (2013c) Stomach cancer incidence statistics. Available from www.cancerresearchuk.org/cancer-info/cancerstats/types/stomach/incidence/

CRUK CancerStats (2013d) Pancreatic cancer incidence statistics. Available from www.cancerresearchuk.org/cancer-info/cancerstats/types/pancreas/incidence/

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