NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Consideration of consultation responses on review proposal

Review of TA179; Sunitinib for the treatment of gastrointestinal stromal tumours

This guidance was issued September 2009 with a review date of August 2011.

Background

At the GE meeting of 8 November 2011 it was agreed we would consult on the review plans for this guidance. A four week consultation has been conducted with consultees and commentators and the responses are presented below.

Proposal put to consultees:	The guidance should be transferred to the 'static guidance list'.[1]
Rationale for selecting this proposal	Since the previous guidance was issued, no new interventions have come to market and the marketing authorisation for sunitinib has not changed. Very limited new evidence has become available and it does not suggest that the TA179 recommendations would change if the appraisal were subject to review. In addition, the manufacturer has no plans to change the existing patient access scheme (PAS) and the Department of Health is content for the PAS to continue in its current format therefore no review of the PAS is required.

GE is asked to consider the original proposal in the light of the comments received from consultees and commentators, together with any responses from the appraisal team. It is asked to agree on the final course of action for the review.

[1] Guidance is placed on the static list when it is clear that there is no new research available that would have any material effect on the current guidance. Topics on the static list may be transferred back to the active list for further appraisal if new evidence becomes available that is likely to have a material effect on the last guidance issued.

Recommendation post consultation:	The guidance should be transferred to the 'static guidance list'.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Novartis	No objection	Further to the email proposing that TA179 be moved to the static list, I confirm that Novartis has no objections to this proposal	Comment noted.
Medicines and Healthcare products Regulatory Agency	No comment	We cannot contribute anything further to the information NICE has reviewed.	Comment noted.
Association of Cancer Physicians	Agree	Thank you for giving us the opportunity to comment on the suggestion that this guidance does not need to be reviewed. I was a clinical expert for the initial technology appraisal in 2009, representing the NCRI Sarcoma Clinical Studies Group, Association of Cancer Physicians and Royal College of Physicians. Since the initial report by Demetri et al (Lancet 2006;368:1329-38) many patients have received sunitinib as second line therapy for GIST progressing on imatinib and it is the standard treatment for this situation world-wide. No other agent has been licensed for this indication since the publication of TA179 and I am not aware of any information to suggest that a review of this guidance would lead to any changes in the current recommendations. I have discussed this response with colleagues in the ACP and at a meeting of the NCRI Sarcoma	Comment noted. Thank you for the update on the establishment of a GIST registry.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
		CSG. Having reviewed the options listed in Appendix 1, for the reasons given above I agree with the proposal that the guidance not be reviewed and that it be transferred to the static guidance list. The accompanying papers refer to the absence of an initiative to establish a GIST Registry. I can confirm that progress is well advanced towards establishing such a project, supported by Novartis. The software has been written, tested and is currently being uploaded onto hospital systems. A protocol has been written and given ethical approval, a Steering Committee, which I chair, has met on a number of occasions to agree standard operating procedures, intellectual property and governance issues and patient data will soon be entered and centrally stored in batches. The centres taking part have access to mutational analysis, which is recognised to be a crucial piece of information in determining prognosis and appropriate treatment in this patient population. I acknowledge that NICE is constrained by the fact that only licensed clinical indications can be considered and within this the licensed dose and schedule are the ones endorsed. However, it is worth pointing out that sunitinib is a difficult drug to use and that optimal results are only obtained by experienced practitioners, often using modified doses and schedules, such as 37.5 mg daily, rather than intermittent administration. Dose intensity needs to be maintained and is as crucial to the success of treatment as it is for imatinib. If further appraisal of this urgent were to be undertaken it would be a lost opportunity if such data were not considered.	

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Healthcare Improvement Scotland	No comment	Healthcare Improvement Scotland has no comment to make on the proposal to move TA179 to the static list.	Comment noted.
GIST Support UK / Sarcoma UK	Agree	We support the proposal to move TAG No 179 to the static list. We recognise that it may again be considered for review whenever new evidence is published or new technologies are registered which may affect the clinical use of sunitinib. We are not aware of research evidence which might significantly alter the rationale on which this Guidance is based. Neither are we aware of current studies using sunitinib which may produce evidence of any significance. We are aware of studies of new agents (underway and planned) which may affect the treatment options for patients with advanced GIST refractory to imatinib. However our understanding is that none of these studies is likely to be published before Q3 2012. We welcomed the call in TAG No 179 for a GIST registry and we regret that one has not yet been set up. There are moves to establish one at an academic centre and we understand that implementation is underway. We welcome the registry and we have declared our wish that retrospective data should be gathered to ensure that the resource can offer value to clinical and regulatory decision-making as soon as possible. We wish to inform NICE of issues regarding current clinical practice relevant to the use of sunitinib for treating GIST so that the Institute is aware of these issues whenever the Guidance is	Comment noted. We note your comments on the current clinical practice for treating GIST and also the value of reviewing TA179 in the future. If there is a proposal to move the guidance from the static list and to review it, there will be an opportunity for comments to be provided on the review proposal.

Respondent	Response to proposal	Details	Comment from Technology Appraisals
		considered for review. The licensed dosing for sunitinib is 50mg/day for four weeks, with two weeks off treatment, making a treatment cycle of 6 weeks. This therapy has side effects which are not well tolerated by a sizable proportion of patients, resulting in dose reductions in the short-term, with some patients withdrawing from treatment, and in long-term dose modification for many patients. Skilled specialist oncologists will work with their patients to find a modified dosing regimen which suits the patient's needs and individual responses to the therapy. As an example we know of several patients taking 37.5mg daily uninterrupted, and of at least one patient on 25mg/37.5mg on alternate days. The extent of such dose modification in practice is unknown but we are aware of patients who were not given the option of dose modification and whose therapy was withdrawn. This emphasises that the Guidance requirement for a cohort of specialist oncologists to treat GIST has not been actioned by the NHS. We call on Commissioners to implement appropriate steps and for NICE to use its influence to ensure that such recommendations are actioned in future. It can be noted that the modified dose approach may deliver patient benefit at a lower gross cost to the NHS than that used in the Appraisal which led to the Guidance. The withdrawal of treatment, rather than attempting to dose modify, by some oncologists, wastes NHS resources and dis-benefits affected patients. Ignoring the issue of side effects management it must be	

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		recognised that patient response to sunitinib is widely variable. Some patients show signs of progression within weeks of commencing sunitinib and some respond for several years (approximately 50 months is the longest of which we are aware in the UK). As genetic mutation analysis is not standard clinical practice in the UK there are no data to indicate whether primary KIT mutations influence response, or whether such variability is down to some other factor(s) (eg secondary mutations). It could lead to an important step forward in treatment if there could be research to identify markers which would allow sunitinib to be more accurately targeted to those patients most likely to respond. As a final comment we would note that manufacturers appear reluctant to apply for registration for modified doses of agents in rare cancers, once those agents have been initially registered. The process of application is time-consuming and costly, there is rarely any benefit in patent life, and specialist oncologists are used to considering research evidence to influence their treatment practice. The NICE process is also a positive disincentive to seek registration because of its costs, uncertainties and bias against rare diseases. Patients become reliant on 'off label' prescribing of modified doses, giving added weight to alternative appraisal/funding approaches. While we accept that under current methods TAG179 may be re-visited by NICE we would question whether any value to patients, the NHS, or society at large would result from such action.	

Respondent	Response to proposal	Details	Comment from Technology Appraisals
Royal College of Physicians / National Cancer Research Institute / Royal College of Radiologists / Association of Cancer Physicians	Agree	The NCRI/RCP/RCR/ACP/JCCO agree with the NICE proposal to move this technology to the static list. As stands, we agree that there are no new relevant data on the use of sunitinib for the treatment of GIST and that the NICE guidance does not need updating.	Comment noted.
Pfizer	Agree	Pfizer welcome and agree with the proposed decision by NICE to transfer TA179 to the static guidance list. This is the right decision as no new significant evidence emerged since original review and marketing authorisation for sunitinib has not changed. In addition, Pfizer have no plans to change the existing patient access scheme.	Comment noted.
Royal College of Nursing	No comment	Nurses caring for people with gastrointestinal conditions were invited to comment on the proposals to move the above health technology appraisal guidance to the static list. There are no comments to make on this proposal on behalf of the Royal College of Nursing.	Comment noted.

No response received from:

Patient/carer groups	General
• Afiya Trust	• Board of Community Health Councils in Wales

- Beating Bowel Cancer
- Black Health Agency
- Bowel Cancer Information
- Bowel Cancer UK
- Cancer Black Care
- Cancer Equality
- Colostomy Association
- Counsel and Care
- Equalities National Council
- Helen Rollason Heal Cancer Charity
- IA (Ileostomy and Internal Pouch Support Group)
- Macmillan Cancer Support
- Maggie's Centres
- Marie Curie Cancer Care
- Muslim Council of Britain
- Muslim Health Network
- Ochre
- Oesophageal Patients Association
- Ostomy Lifestyle Centre
- Rarer Cancers Foundation
- South Asian Health Foundation
- Specialised Healthcare Alliance
- Stomach Cancer Awareness Network
- Tenovus

<u>Professional groups</u>

- Association of Coloproctologists of Great Britain
- Association of Surgeons of Great Britain and Ireland
- Bladder and Bowel Foundation
- British Association for Services to the Elderly
- British Association of Surgical Oncology
- British Geriatrics Society
- British Institute for Radiology
- British National Formulary
- Care Quality Commission
- Commissioning Support Appraisals Service
- Department of Health, Social Services and Public Safety for Northern Ireland
- National Association of Primary Care
- National Pharmacy Association
- NHS Alliance
- NHS Commercial Medicines Unit
- NHS Confederation
- Public Health Wales NHS Trust
- Scottish Medicines Consortium

<u>Relevant research groups</u>

- Bowel & Cancer Research
- CORE (Digestive Disorders Foundation)
- Institute of Cancer Research
- MRC Clinical Trials Unit
- National Cancer Research Network
- National Institute for Health Research
- Research Institute for the Care of Older People

<u>Assessment Group</u>

- National Institute for Health Research Health Technology Assessment Programme

<u>Associated Guideline Groups</u>

- National Collaborating Centre for Cancer

<u>Associated Public Health Groups</u>

- None

• British Psychosocial Oncology Society • British Society of Gastroenterology • Cancer Network Pharmacists Forum • Cancer Research UK • Pelican Cancer Foundation • Royal College of Anaesthetists • Royal College of General Practitioners • Royal College of Pathologists • Royal College of Surgeons • Royal Pharmaceutical Society • Royal Society of Medicine • Society and College of Radiographers • United Kingdom Clinical Pharmacy Association • United Kingdom Oncology Nursing Society <u>Others</u> • Department of Health • NHS Brighton and Hove • NHS Bristol • Welsh Government	

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22 December 2011