NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

GUIDANCE EXECUTIVE (GE)

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

This guidance was issued in September 2009.

The review date for this guidance is August 2011.

1. Recommendation

The guidance should be transferred to the 'static guidance list'. That we consult on this proposal.

2. Original remit(s)

To appraise the clinical and cost effectiveness of sunitinib within its licensed indication for the treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumours**.**

3. Current guidance

1.1 Sunitinib is recommended, within its licensed indication, as a treatment option for people with unresectable and/or metastatic malignant gastrointestinal stromal tumours if:

- imatinib treatment has failed because of resistance or intolerance, and
- the drug cost of sunitinib (excluding any related costs) for the first treatment cycle will be met by the manufacturer.

1.2 The use of sunitinib should be supervised by cancer specialists with experience in treating people with unresectable and/or metastatic malignant gastrointestinal stromal tumours after failure of imatinib treatment because of resistance or intolerance.

4. Rationale[1]

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)

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

and the Department of Health is content for the PAS to continue in its current format therefore no review of the PAS is required.

5. Implications for other guidance producing programmes

There is no proposed or ongoing guidance development that overlaps with this review proposal.

6. New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from December 2007 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

Since the previous guidance was issued, no new interventions have come to market and the marketing authorisation for sunitinib has not changed.

The updated literature searches for sunitinib for the treatment of unresectable and/or metastatic malignant gastrointestinal stromal tumours (GIST) identified very limited new evidence.

A phase II study assessed continuous daily doses of sunitinib dosing in patients with imatinib-resistant/intolerant GIST (George 2009). The patients were randomised to receive morning or evening dosing of sunitinib 37.5 mg/day. The clinical benefit rate (percent complete responses + partial responses + stable disease at 24 weeks) was 53: eight patients (13%) achieved objective partial responses and 24 (40%) achieved stable disease at 24 weeks. Median PFS was 34 weeks; median OS was 107 weeks. In summary, the results of this study support the original conclusion of technology appraisal 179.

A phase IIIb study of sunitinib versus imatinib for the treatment of patients with GIST who have had progressive disease while on imatinib was initiated but was prematurely discontinued in July 2009 due to poor recruitment as a result of changes in clinical practice. No other new studies have been identified.

This new evidence does not suggest that the recommendations would change if the appraisals were subject to review.

Patient Access Scheme

The manufacturer has no plans to change the existing patient access scheme (PAS) and is proposing to continue to provide the first cycle of sunitinib free to the NHS. The DH is content for the PAS to continue in its current format.

8. Implementation

A submission from Implementation is included in Appendix 3.

Data calculated by IMS that indicated that the volume of prescribing of sunitinib remained the same in the months following the publication of TA179. However, these data do not link to diagnosis and so should be treated with caution.

9. Equality issues

No equality issues were identified.

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Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A review of the guidance should be planned into the appraisal work programme.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment

- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed

- The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

TA209 Imatinib for the treatment of unresectable and/or metastatic gastrointestinal stromal tumours. Published November 2010, review date August 2013. This is a part review of NICE technology appraisal guidance 86 (Oct 04)

NB TA209 has a research recommendation relevant to TA179:

- A national register should be maintained for all people with gastrointestinal stromal tumours (GISTs) being treated with imatinib, sunitinib and best supportive care (to support future appraisals of treatments for this patient group). Details should include patient characteristics, dose and duration of treatment, tumour response rates and survival, both with and after discontinuation of treatment.

Searching has not revealed the establishment of such a national register.

TA196 Imatinib for the adjuvant treatment of gastrointestinal stromal tumours. Published August 2010, review date June 2011 (due to a potentially relevant trial)

In progress

None found.

Suspended/terminated

None found.

In topic selection[2]

[redacted]

[2] Information held by the NICE Topic Selection Team is treated as being potentially commercially sensitive by default. Details of the topics considered by NICE's Consideration Panels may be available on the NICE website, providing the manufacturers of the technologies under discussion have consented to the release of this information.

[redacted]

Details of changes to the indications of the technology

Indication considered in original appraisal	Proposed indication (for this appraisal)
Sunitinib has a UK marketing authorisation for the treatment of people with unresectable and/or metastatic malignant gastrointestinal stromal tumour (GIST) after failure of imatinib mesilate treatment due to resistance or intolerance.	Unchanged.

Details of new products

Drug (manufacturer)	Details (phase of development, expected launch date)
None found for second line treatment of GIST, however there are two third line technologies in the pipeline but not close to marketing authorisation. One is regorafenib, which is in phase III development and has been fast tracked by the FDA (May 11) [redacted] The other, sorafenib, is in phase II recruitment stage (NCT00265798 and NCT01091207)	

Registered and unpublished trials

Trial name and registration number	Details
Phase IV trials in progress: NCT00793871 NCT01073644 NCT00716820 NCT00444795	These are unlikely to materially affect guidance in TA179
Phase III: NCT00428220	This is unlikely to materially affect guidance in TA179 as it's a treatment continuation protocol

References

George S, Blay JY, Casali PG et al. (July 2009) Clinical evaluation of continuous daily dosing of sunitinib malate in patients with advanced gastrointestinal stromal tumour after imatinib failure. *European Journal of Cancer.* 45 (11): 1959-1968.

Appendix 3 – Implementation submission

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

IMPLEMENTATION PROGRAMME

Guidance Executive Review

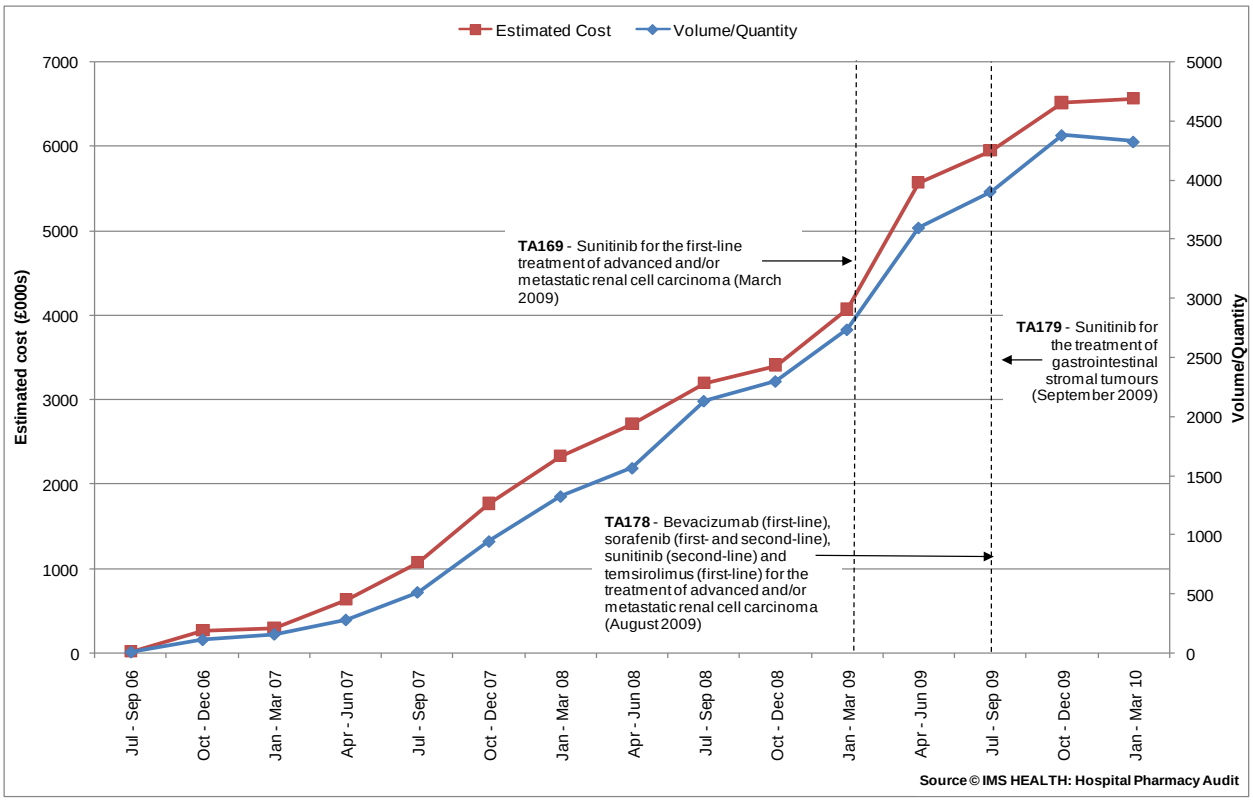
Technology appraisal 179: Sunitinib for the treatment of gastrointestinal stromal tumours

1. Routine healthcare activity data

This section provides information on prescribing estimated cost and volume for drugs issued in hospitals in England. The data are obtained from the IMS HEALTH Hospital Pharmacy Audit Index. All costs stated in this report are based on estimated cost.

1.1 IMS HEALTH Hospital Pharmacy Audit Index (HPAI) – sunitinib

Figure 1 Trend in the cost and volume of prescribing sunitinib in hospitals in England



The above chart shows that there was no significant change in the rate of prescribing costs and volume for sunitinib following the publication of NICE technology appraisal 179. In the first quarter of 2010 the prescribing cost for sunitinib was £6,561,952 with a corresponding volume of 4325 items. The data shows that prescribing cost and volume appears to have reached a plateau. It is unclear yet whether this is a temporary or ongoing trend.

This data must also be interpreted with caution as data are not linked to diagnosis. It is therefore not possible to ascertain what proportion of prescribing of sunitinib relates to patients with gastrointestinal stromal tumours.

Notes:

- The IMS HEALTH Hospital Pharmacy Audit Index (IMS HPAI) collects information from pharmacies in hospital trusts in the UK. The IMS HPAI database is based on 'issues' of medicines recorded on hospital pharmacy systems. 'Issues' refer to all medicines supplied from hospital pharmacies to: wards; departments; clinics; theatres; satellite sites and to patients in outpatient clinics and on discharge.

- Volume/Quantity: This is the number of packs of a medicine that are issued. They should not be added together due to differences in dosages/pack sizes.

- Cost (in £s): Estimated costs are calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost. Costs based on the drug tariff provide a degree of standardization allowing comparisons of prescribing data from different sources to be made. The costs stated in this report do not represent the true price paid by the NHS on medicines. The estimated costs are used as a proxy for utilization and are not suitable for financial planning.

2. External literature

There is currently no literature relating to the uptake of technology appraisal 179.