Appendix G – patient/carer organisation statement template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of TA196)

Thank you for agreeing to give us your views on the technology and the way it should be used in the NHS.

Patients and patient advocates can provide a unique perspective on the technology, which is not typically available from the published literature.

To help you give your views, we have provided a template. The questions are there as prompts to guide you. You do not have to answer every question. Please do not exceed the 8-page limit.

About you

Your name: [redacted] **and** [redacted]

Name of your organisation: Sarcoma UK

Are you (tick all that apply):

- a patient with the condition for which NICE is considering this technology?
- a carer of a patient with the condition for which NICE is considering this technology?
- an employee of a patient organisation that represents patients with the condition for which NICE is considering the technology? If so, give your position in the organisation where appropriate (e.g. policy officer, trustee, member, etc) [redacted] is [redacted]
- other? (please specify) [redacted] is [redacted] – [redacted]

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of TA196)

What do patients and/or carers consider to be the advantages and disadvantages of the technology for the condition?

1. Advantages

(a) Please list the specific aspect(s) of the condition that you expect the technology to help with. For each aspect you list please describe, if possible, what difference you expect the technology to make.

The response of GIST to imatinib for the large majority of patients is well documented and understood. Its use as first-line therapy in the unresectable/metastatic setting is covered by NICE TA86. Long term response is possible, second-line and third-line therapies are available, surgical excision of metastases is now considered for responding patients, median overall survival is of the order of 5 years.

It is now clear that the critical clinical point on the patient pathway is the first resistance to imatinib in first-line therapy. This is the point at which therapy has to take a palliative approach, the aim no longer being cure but the extension of life which is under active threat. Delaying the point of first resistance has now been shown to have a beneficial impact on overall survival, as well as meaning that patients treated this way will have a longer period of life with a high-quality of life.

Adjuvant imatinib addresses this opportunity. The studies have demonstrated that patients receiving one year of adjuvant imatinib have a longer period to recurrence than those receiving placebo (ACOSOG Z9001 study) and although OS data is not available (there was a cross-over which prevents later analysis) we have sufficient data from clinical practice to suggest an improvement in OS as a result. In later analysis an absolute benefit for those within the high risk category was identified.

The benefits of three years versus one year of adjuvant imatinib (the SSGXVIII/AIO study) are equally clear with an improved interval before relapse for the group treated for three years. An OS advantage was also demonstrated. Both groups in this study showed a tendency to relapse once adjuvant therapy ceased and this finding raises questions as to whether recurrence is being prevented or just delayed by the therapy.

We await full results of a third study (EORTC 62024) which used onset of resistance to first-line imatinib as its principle endpoint.

The use of adjuvant imatinib is recommended by EMA and FDA for patients at ‘high risk’ of relapse. Prior to adjuvant therapy a significant proportion of high risk patients relapsed within months of primary surgery. They were the ones at highest risk of not reaching the (then) median survival of 5 years. Assessing who is at ‘high risk’ is therefore a crucial component of the use of adjuvant imatinib. Research has demonstrated a relatively simple approach based on tumour location, size, mitotic count and nature of surgery. The risk model most widely used is that published by Meittenen & Lasota. Research continues and we anticipate that this model will be overtaken by developments, especially as genetic profiling is increasingly applied to the problem.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of TA196)

The advantage of adjuvant imatinib is that it delays the onset of resistance to imatinib. By definition, after surgery the patient has no evidence of active disease and the secondary mutations which cause resistance are prevented from activating by the therapy. The quality of life lived on adjuvant imatinib is largely indistinguishable from normal daily life, any functional disabilities will be those caused by the surgery for the primary tumour.

(The number of publications is small and references will be provided by the submission made through the Royal College of Physicians, as also no doubt by the manufacturer).

(b) Please list any short-term and/or long-term benefits that patients expect to gain from using the technology. These might include the effect of the technology on:
- the course and/or outcome of the condition
- physical symptoms
- pain
- level of disability
- mental health
- quality of life (lifestyle, work, social functioning etc.)
- other quality of life issues not listed above
- other people (for example family, friends, employers)
- other issues not listed above

The benefits for patients who have just completed surgery for a primary GIST are the fact that there is a practical treatment which helps prevent the cancer returning in the medium/short-term. This is also psychologically reassuring. Imatinib is an oral tablet, taken once a day. Its impact on the patient's routine of life is minimal.

It allows people to return to a 'normal' life. Constraints are usually those which result from the preceding surgery not from the adjuvant therapy. Those of working age are often able to return to work, their lifestyle and quality of life largely unaffected by the diagnosis and treatment.

For some there is the awareness that the therapy will stop in the longer term (three years) and that the disease may return but many put this concern to one side.

2. Disadvantages

Please list any problems with or concerns you have about the technology. Disadvantages might include:
- aspects of the condition that the technology cannot help with or might make worse
- difficulties in taking or using the technology
- side effects (please describe which side effects patients might be willing to accept or tolerate and which would be difficult to accept or tolerate)
- impact on others (for example family, friends, employers)
- financial impact on the patient and/or thier family (for example cost of travel needed to access the technology, or the cost of paying a carer)

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of TA196)

Imatinib is generally well tolerated and the therapy required to control side-effects well understood by doctors, nurses and patient support groups. Patients with side-effects when the drug is first introduced usually settle down quickly. In a few cases some dose adjustment may be necessary but these cases are rare and the dose adjustment usually short-term.

3. Are there differences in opinion between patients about the usefulness or otherwise of this technology? If so, please describe them.

We have no evidence that any GIST patient disagrees with the use of adjuvant imatinib. Those first treated some years ago when the therapy was not available are often quietly envious of more recent patients who they perceive as being given an opportunity for longer life than they have been given.

4. Are there any groups of patients who might benefit **more** from the technology than others? Are there any groups of patients who might benefit **less** from the technology than others?

Although genetic analysis of GIST has identified a number of groups whose tumour characteristics indicate better/worse response to imatinib at different dosing levels there is currently no definitive indication that any of these groups will benefit more or less from adjuvant therapy. A small number of very rare primary mutations (eg. PDGFRA exon18 D842V) show no response to imatinib in first-line but whether a patient might benefit from adjuvant therapy following complete resection is unknown.

Comparing the technology with alternative available treatments or technologies

NICE is interested in your views on how the technology compares with existing treatments for this condition in the UK.

(i) Please list any current standard practice (alternatives if any) used in the UK.

There is no alternative therapy. At one time all patients, and today patients not at a ‘high risk’, are monitored on a ‘watch and wait’ basis. The latter are at a lower risk of relapse but a percentage of those with a ‘medium risk’ do relapse with metastases and require first-line imatinib therapy. Those at ‘low risk’ are unlikely to relapse.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of TA196)

(ii) If you think that the new technology has any **advantages** for patients over other current standard practice, please describe them. Advantages might include:
- improvement of the condition overall
- improvement in certain aspects of the condition
- ease of use (for example tablets rather than injection)
- where the technology has to be used (for example at home rather than in hospital)
- side effects (please describe nature and number of problems, frequency, duration, severity etc)

There are no alternative therapies for adjuvant imatinib other than 'watch and wait'. We anticipate that research into risk patterns will reduce the number of patients classified as of 'medium risk', who would currently be on a 'watch and wait' protocol. This is subject to research.

(iii) If you think that the new technology has any **disadvantages** for patients compared with current standard practice, please describe them. Disadvantages might include:
- worsening of the condition overall
- worsening of specific aspects of the condition
- difficulty in use (for example injection rather than tablets)
- where the technology has to be used (for example in hospital rather than at home)
- side effects (for example nature or number of problems, how often, for how long, how severe).

There are no disadvantages for patients who receive adjuvant imatinib. They can expect to live a longer and fuller life.

Research evidence on patient or carer views of the technology
If you are familiar with the evidence base for the technology, please comment on whether patients' experience of using the technology as part of their routine NHS care reflects that observed under clinical trial conditions.

In 2009 we conducted a short quality of life study using the EuroQol EQ-5D with a group of 43 GIST patients at all stages in the treatment pathway. Of these 34 were receiving TKIs. The participants were asked to complete the EQ-5D as at the current date.

Median age: 57 (range 34-74)
Overall median utility score: 0.761 (range 0.238 – 1.00)
Overall EQ-VAS score: 89/100 (range 33-100)

Other utility scores:
Had surgery only (5 patients): 0.74
Receiving adjuvant imatinib (2): 0.73
Receiving standard dose imatinib (23): 0.78
Receiving high dose imatinib (5): 0.76
Receiving sunitinib (3): 0.67
Receiving nilotinib (third line or later)(3): 0.66

Although the numbers are small there is clear indication of the tolerability of imatinib in that those who had not relapsed/metastasised had a similar score to those on first-line therapy. As expected there is a drop between first and later lines of therapy.

We had no baseline of prior data from the time of diagnosis with which to draw comparisons. We decided to conduct the questionnaire part of the EQ-5D a second time (later in the day) asking people to recall their situation at the time of diagnosis. The overall utility value mean improvement between day of diagnosis and the day of the meeting was 0.192

Other improvements over the baseline at time of diagnosis were:
Mean difference on standard dose imatinib: +0.226
Mean difference on high dose imatinib: +0.318
Mean difference on sunitinib: +0.037
Mean difference on nilotinib: -0.124

We recognise that this approach is methodologically challenging but felt it appropriate when we saw the utility values that resulted. There is a consistency in the pattern which indicates that even with second-line therapy (often 5+ years after diagnosis) patients have a high quality of life.

This small study was early in the life of adjuvant imatinib and only two patients were on this therapy. Their overall scores did not differ significantly from those taking imatinib in first-line. The Pain and Anxiety components of the EQ-5D questionnaire are the ones which attract the lowest assessment from patients.

Are there any adverse effects that were not apparent in the clinical trials but have come to light since, during routine NHS care?

None.

The long term effects of imatinib (some patients are now in year 14) are subject to patient group research at the moment by Sarcoma Patients Euronet and the US-

based LifeRaft Group. As these patients would have died years ago without imatinib it is not thought that results will have any value other than to guide ongoing treatment.

Are you aware of any research carried out on patient or carer views of the condition or existing treatments that is relevant to an appraisal of this technology? If yes, please provide references to the relevant studies.

None known.

Availability of this technology to patients in the NHS

What key differences, if any, would it make to patients and/or carers if this technology was made available on the NHS?

This technology is currently available to NHS patients in England through the Cancer Drugs Fund.

It is not routinely available in NHS Wales or in Northern Ireland but has been known to be funded exceptionally.

SMC approved this indication for NHS Scotland in April 2012.

A single approach which is uniform throughout the NHS is necessary.

What implications would it have for patients and/or carers if the technology was **not** made available to patients on the NHS?

Currently the UK is the only place in the Western world where adjuvant imatinib is not routinely available for all 'high risk' patients. We already see patients in Wales 'moving' to live with relatives in England in order to gain access through the Cancer Drugs Fund. This kind of situation makes us a laughing-stock at international events.

Are there groups of patients that have difficulties using the technology?

None that we are aware.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of TA196)

Equality
NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that this appraisal:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which [the treatment(s)] is/are/will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could lead to recommendations that have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

None that we are aware.

Other Issues
Please consider here any other issues you would like the Appraisal Committee to consider when appraising this technology.

An important part of the procedure for prescribing adjuvant imatinib is the classification of 'high risk'. Over the last five years there have been a number of assessment 'tools' developed. The one currently in widest use is the one published by Meittenen & Lasota. This should not be regarded as the only tool which is possible, or as the best which will ever become available.

The prescribing of adjuvant imatinib should be subject to use of an evidence-based, published and peer-reviewed assessment tool. It can be anticipated that consensus meetings of ESMO, the British Sarcoma Group or under the aegis of other professional associations, will review and agree on future proposed assessment aides. The FAD (assuming recommendation to accept adjuvant imatinib) should make it clear that best clinical practice should be followed, and it should not dictate that guidance from a specific assessment tool is required.

We have consulted with patients, specialist clinicians, the Royal College of Physicians, the NCRI Clinical Studies Group and the British Sarcoma Group in preparing this submission.