Appendix G – patient/carer organisation statement template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Trastuzumab emtansine for treating HER2-positive, locally advanced or metastatic breast cancer after treatment with trastuzumab and a taxane

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]

Name of your organisation: Breakthrough Breast Cancer

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)

  Senior Policy Officer

- other? (please specify)

Appendix G – patient/carer organisation statement template

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Trastuzumab emtansine for treating HER2-positive, locally advanced or metastatic breast cancer after treatment with trastuzumab and a taxane

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.

This appraisal is considering trastuzumab emtansine (T-DM1) for treating HER2+, locally advanced or metastatic breast cancer after treatment with trastuzumab and a taxane. The treatment options for women with this form of the disease are limited and typically involve chemotherapy and the targeted anti-HER2+ therapy trastuzumab. However, this treatment only delays disease progression by around 12 months, following which patients are usually treated with non-targeted chemotherapies such as capecitabine or vinorelbine. Lapatinib, a HER2+ targeted therapy, is licensed for this stage of the treatment pathway but has not been approved by NICE.

T-DM1 is an antibody-drug conjugate which has been compared to treatment with lapatinib plus capecitabine in the EMILIA trial[i]. T-DM1 is composed of trastuzumab, a monoclonal antibody which inhibits HER2 signalling and stimulates the immune system to destroy the cell, conjugated by a stable linker to DM1, a potent cytotoxic agent which leads to cell death. This allows the targeting of DM1 to cells over-expressing the HER2 receptor, where it is internalised and released from the stable linker. In this way, the dual actions of trastuzumab and DM1 are targeted specifically to cells over-expressing the HER2 receptor, whilst reducing exposure of normal tissues to the drugs.

This is the first drug of its kind for breast cancer and is extremely innovative, providing significant improvements in outcomes for patients, whilst minimising the systemic side-effects which are usually associated with chemotherapy.

(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

Results from the EMILIA trial show a 5.8 month increase in overall survival, from 25.1 months with lapatinib plus capecitabine, to 30.9 months with T-DM1. Progression free survival was increased by 50%, from 6.4 months to 9.6 months.

Importantly, results from the trial also indicate an increase in the patient-reported time to symptom progression, from 4.6 months to 7.1 months, and a more favourable quality of life for patients being treated with T-DM1. Patients in the T-DM1 arm were significantly less bothered by side effects throughout their treatment time than those being treated with lapatinib and capecitabine[ii].

Adverse events in the T-DM1 arm were primarily for laboratory measured outcomes (thrombocytopenia and increased serum aminotransferase) rather than the typical side effects associated with chemotherapy which would be expected to impact significantly on quality of life (diarrhoea, nausea, vomiting, palmar-plantar erythrodysesthesia). A greater number of patients required dose reduction due to adverse events in the lapatinib plus capecitabine arm compared to the T-DM1 arm, suggesting that T-DM1 is well tolerated and has a favourable toxicity profile[i].

We know that patients with locally recurrent or metastatic breast cancer place huge value treatments that can control their cancer, delay disease progression, and extend their lives. T-DM1 provides a clear survival benefit which can make a major difference to the lives of metastatic breast cancer patients. Remarkably, this clear survival benefit does not come at the cost of quality of life, and the drug has been shown to actually improve quality of life measures. This is hugely significant for patients with metastatic breast cancer, for whom it is vitally important that improved clinical outcomes do not come at the expense of quality of life.

"Simply put, length of life is only worth having if there is quality of life as well."

Breakthrough Supporter and Metastatic Breast Cancer Patient

The goal of treatment for metastatic breast cancer, which is an incurable disease, is to allow patients to live as well as possible for as long as possible, and T-DM1 represents a major step forward for this patient group.

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)

T-DM1 is administered intravenously whereas lapatinib and capecitabine are taken orally and therefore do not require a hospital visit for administration. Some patients may prefer to take their medication orally, at home, rather than being required to travel to hospital for intravenous treatment. However, regular hospital visits are still required when being treated with lapatinib and capecitabine in order to monitor treatment-related side effects. We know

from speaking to patients with metastatic breast cancer that treatments which extend their lives and allow them to continue to live as well as possible for as long as possible are hugely important to them, so it is likely that the majority of patients would not feel that the requirement for intravenous administration would outweigh the benefits of the drug.

As explained in question 2b, the side effects associated with T-DM1 are primarily laboratory measured outcomes rather than symptoms which are typically associated with chemotherapy treatment, and which would be expected to have significant adverse effects on quality of life. In the EMILIA trial, incidences of thrombocytopenia and increased serum aminotransferase were higher in the T-DM1 arm whereas diarrhoea, nausea, vomiting, and palmar-plantar erythrodysesthesia were all higher in the lapatinib plus capecitabine arm[i]. Patients treated with T-DM1 reported being significantly less bothered by side effects than those in the lapatinib plus capecitabine arm[ii], suggesting that, whilst there are side effects associated with T-DM1treatment, these are well tolerated.

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

Patients will differ in their treatment preferences and in their response to treatment, in terms of both clinical and quality of life outcomes. It is therefore important that the risks and benefits of each treatment choice are explained fully to patients and that their clinical response and quality of life are monitored carefully. However, based on what patients with metastatic breast cancer have told us is important to them, we would expect this technology to be strongly welcomed by patients.

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?

T-DM1 is only suitable for patients with HER2+ disease as it is a targeted therapy directed at the HER2 receptor. HER2+ breast cancer is often described as being particularly aggressive and the only targeted therapy which has been approved by NICE for use in these patients is trastuzumab. T-DM1 is therefore likely to result in substantial benefits in treatment outcome for this group of patients, for whom options when progression after trastuzumab therapy occurs are limited to standard, untargeted chemotherapy, in the absence of routine lapatinib use.

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.

NICE clinical guideline CG81 recommends the use of non-targeted chemotherapy (capecitabine or vinorelbine) after disease progression on trastuzumab therapy and states that trastuzumab therapy should be discontinued unless disease progression is in the central

nervous system alone. In clinical practice trastuzumab therapy may be continued in combination with capecitabine or vinorelbine.

Lapatinib is also licensed for use in combination with capecitabine at this stage of the treatment pathway, although it has not been approved by NICE for routine use in the NHS. It is therefore important to note that the availability of lapatinib is dependent on its continued availability of the Cancer Drugs Fund and is not considered to be a standard treatment which is available routinely in the NHS.

(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)

As described in the responses to questions 1a and 1b, treatment with T-DM1 provides significant PFS and OS benefits for patients, with minimal side effects. In particular, the side effects associated with T-DM1 treatment are different to those normally associated with chemotherapy treatment, and appear to be well tolerated, so are likely to impact less on patients' quality of life. This will allow patients to live as well as possible for as possible.

"When people know they have a terminal diagnosis every day extra is so important. This has to be balanced by the impact on their quality of life. If the drug causes too many side effects the additional time gained may not be the quality time they need."

Breakthrough Supporter and Metastatic Breast Cancer Patient

(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).

As described in the response to question 2, T-DM1 is administered via IV, whereas lapatinib and capecitabine are administered orally. Vinorelbine can be administered orally or via IV and trastuzumab is administered by IV. Some patients may prefer oral medications to those administered by IV but this is unlikely to represent a significant disadvantage when compared to the advantages of T-DM1 for most patients.

Some side-effects are more common in patients treated with T-DM1 (thrombocytopenia and increased serum aminotransferase) but these are unlikely to have a significant impact on patients' quality of life. The side effects associated with the alternative treatments (diarrhoea, nausea, vomiting, and palmar-plantar erythrodysesthesia) are more likely to have a detrimental impact on quality of 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.

T-DM1 has only recently been licensed for use in Europe (license granted 20th November 2013), and has not yet been considered for inclusion on the Cancer Drugs Fund list, so we are unaware of any patients who will have received the drug outside of a clinical trial setting.

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

None that we are aware of.

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 that we are aware of.

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?

Metastatic breast cancer is an incurable condition and the goal of treatment is to prolong life and to palliate symptoms, in order to allow patients to live as well as possible for as long as possible. The introduction of T-DM1 into the treatment pathway for patients with HER2+ metastatic breast cancer would be a significant step forward for patients with this aggressive form of the disease. The improvements in progression free survival and overall survival are significant and are associated with a reduction in the types of side effects likely to impact substantially on quality of life, when compared to existing treatments. The introduction of targeted therapies for HER2+ breast cancer is particularly important as the only HER2-targeted drug approved for routine use on the NHS is trastuzumab, which most patients will develop resistance to within approximately 12 months.

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

Advances in the treatment of metastatic breast cancer usually involve incremental improvements which over time result in significant increases in how long the disease can be controlled for, and in the quality of life of patients being treated. T-DM1 represents

improvements in these measures which are more substantial than those usually seen, and it is crucial that patients are able to access the drug routinely on the NHS so that they can benefit from these advances. Breakthrough, and the patients we represent, would be hugely disappointed if a drug such as T-DM1 were not to be approved, and it would indicate a very uncertain future for breast cancer treatment in the UK.

T-DM1 is now considered to be standard second line treatment for HER2+ metastatic breast cancer in the US and if we are unable to allow patients to have routine access to these kinds of drugs in the UK then we risk falling behind international standards of care for the treatment of breast cancer. This is particularly concerning because the only alternative HER2+ targeted treatment licensed for use at this stage of the treatment pathway, lapatinib, is not routinely available in the NHS. Should T-DM1 not be approved, these will be two steps towards improved outcomes for HER2+ metastatic breast cancer patients that we will not have taken in the UK. Furthermore, we risk that future clinical trials will not be carried out in the UK as they will be comparing or combining new drugs with existing drugs such as T-DM1 which are considered to be standard of care elsewhere, or investigating new drugs in patients who have been previously treated with existing drugs such as T-DM1.

If NICE is unable to approve this drug it would represent a significant step back for breast cancer treatment in the UK. We urge the Committee and the manufacturer to work together, and with other stakeholders, to ensure UK breast cancer patients are able to access the most effective treatment for their condition.

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

None that we are aware of

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.

N/A

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal (STA)

Trastuzumab emtansine for treating HER2-positive, locally advanced or metastatic breast cancer after treatment with trastuzumab and a taxane

Other Issues

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

T-DM1 is a very effective drug that has the potential to change the lives of women with metastatic breast cancer. This is the third extremely innovative breast cancer drug that NICE have assessed this year - in August NICE was unable to approve everolimus in combination with exemestane and issued an ACD not recommending pertuzumab in combination with trastuzumab.

Value-based pricing, due to be introduced in Autumn 2014, was originally intended to promote innovation, ensure better access to effective drugs and improve value for money for the NHS. However, the proposals for value-based pricing have since been drastically watered down and Breakthrough Breast Cancer is concerned that value-based pricing will not address the issue, highlighted by the recent decisions described above, of routine access to effective cancer drugs, and will not allow NICE to approve promising drugs such as T-DM1. This would represent a huge setback for metastatic breast cancer patients in the UK and Breakthrough would welcome further clarity on this issue from the relevant stakeholders.

---

[i] Verma S *et al.* (2012), Trastuzumab emtansine for HER2-positive advanced breast cancer, N Engl J Med. 2012 Nov 8;367(19):1783-91

[ii] Welslau M *et al.*(2013), Patient-reported outcomes from EMILIA, a randomized phase 3 study of trastuzumab emtansine (T-DM1) versus capecitabine and lapatinib in human epidermal growth factor receptor 2-positive locally advanced or metastatic breast cancer, Cancer. 2013 Nov 12