Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Multiple Technology Appraisal

Lenvatinib and sorafenib for treating differentiated thyroid cancer after radioactive iodine

Draft scope

Remit/appraisal objective
To appraise the clinical and cost effectiveness of lenvatinib and sorafenib within their marketing authorisations for treating differentiated thyroid cancer after radioactive iodine.

Background
Thyroid cancer can be ‘differentiated’ or ‘undifferentiated’. ‘Differentiated’ thyroid cancer cells still retain the appearance of normal thyroid cells and they do not spread as rapidly as the undifferentiated type of cancer cells. There are four main types of thyroid cancer; papillary, follicular, medullary and anaplastic; Papillary and follicular carcinomas are differentiated thyroid cancers, and they are similar in both management and prognosis. There are also several less common variants of differentiated thyroid cancer, including but not limited to Hürthle cell, tall cell, insular, and columnar.

Thyroid cancer is uncommon and makes up less than 1% of cancer cases in the UK. Differentiated thyroid cancers are the most common type of thyroid cancer, with papillary carcinomas accounting for approximately 60% - 85% and follicular carcinomas accounting for approximately 5% - 15% of cases. Differentiated thyroid cancers are typically curable with an overall 10-year survival rate of around 90%. Differentiated thyroid cancers which are localised to the thyroid (stage I-III) have the best prognosis with a 10-year relative survival of around 99%. Once the cancer has spread beyond the thyroid (stage IV) the 10-year survival drops to around 63% - 76% depending on the degree of metastasis.

The British Thyroid Association’s ‘Guidelines for the management of thyroid cancer’ outlines treatment options for differentiated thyroid cancer which include surgery, chemotherapy and radiotherapy. Surgery is most common with the aim of removing some or all of the thyroid gland (and sometimes the lymph nodes). Radioactive iodine ablation can be provided after surgery to destroy any remaining cancer cells whilst external beam radiotherapy and chemotherapy are used for palliative care in the small proportion of patients where further surgery or radioiodine is ineffective or impractical. The guideline notes that the use of external beam radiotherapy and chemotherapy in palliative care has begun to be superseded in clinical practice by targeted therapies, which includes sorafenib and lenvatinib. Sorafenib is available from the cancer drug fund for metastatic or inoperable papillary and follicular thyroid cancer, which is refractory to radioiodine.
The technology
Lenvatinib (Lenvima, Eisai) inhibits multiple receptor tyrosine kinases including vascular endothelial growth factor (VEGF) receptors 1-3, fibroblast growth factor (FGF) receptors 1-4, Platelet-derived growth factor (PDGF) receptor alpha, c-KIT, and RET. Lenvatinib is given orally and has a marketing authorisation in the UK for the treatment of adult’s with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma (DTC), refractory to radioactive iodine (RAI).

Sorafenib (Nexavar, Bayer HealthCare) inhibits multiple receptor tyrosine including vascular endothelial growth factor (VEGF) receptors 2-3, Platelet-derived growth factor (PDGF) receptor beta, FLT-3 and c-KIT. It also inhibits the activity of the serine/threonine kinases c-Raf and b-Raf. Sorafenib is given orally and has a marketing authorisation in the UK for the treatment of people with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma, refractory to radioactive iodine.

| Intervention(s) | • Lenvatinib  
|                | • Sorafenib   |
| Population(s)  | Adults with progressive, locally advanced or metastatic, differentiated thyroid carcinoma, refractory to radioactive iodine (RAI). |
| Comparators    | • The interventions listed above will be compared with each other  
|                | • Best supportive care including external beam radiotherapy and chemotherapy |
| Outcomes       | The outcome measures to be considered include:  
|                | • overall survival  
|                | • progression-free survival  
|                | • response rate  
|                | • adverse effects of treatment  
|                | • health-related quality of life |
| Economic analysis | The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.  
The reference case stipulates that 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. Costs will be considered from an NHS and Personal Social Services perspective.

**Other considerations**

Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.

**Related NICE recommendations and NICE Pathways**

- **Related Technology Appraisals:**
  - Cabozantinib and vandetanib for treating unresectable locally advanced or metastatic medullary thyroid cancer. NICE technology appraisals guidance [ID56]. Publication expected January 2018.

- **Related Quality Standards:**

- **Related NICE Pathways:**
  - Head and neck cancer NICE pathway

**Related National Policy**

- **NHS England**

- **National Service Frameworks**
  - Cancer

- **Other policies**

**Questions for consultation**

Have all relevant comparators for lenvatinib and sorafenib been included in the scope?
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Which treatments are considered to be established clinical practice in the NHS for treating differentiated thyroid cancer after radioactive iodine?

- are other targeted therapies used in clinical practice for treating differentiated thyroid cancer after radioactive iodine?
- what best supportive care options for people with this disease are used in clinical practice?

Where do you consider lenvatinib and sorafenib will fit into the treatment pathway for differentiated thyroid cancer?

- would people only be considered for treatment with lenvatinib or sorafenib after radioactive iodine if the disease was inoperable?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom lenvatinib and sorafenib are expected to be more clinically effective and cost effective or other groups that should be examined separately?

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 the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which lenvatinib and sorafenib are 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 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.

Do you consider lenvatinib and sorafenib to be innovative in their potential to make a significant and substantial impact on health-related benefits and how they might improve the way that current need is met (are these a ‘step-change’ in the management of the condition)?
Do you consider that the use of lenvatinib and sorafenib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

References
4. Types of thyroid cancer. NHS choices [accessed August 2016]