

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Multiple Technology Appraisal**

**Lenvatinib and sorafenib for treating differentiated thyroid cancer after radioactive iodine**

**Final 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<sup>1</sup>. 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<sup>2</sup>.

Thyroid cancer is uncommon and makes up less than 1% of cancer cases in the UK<sup>3</sup>. 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<sup>4,5</sup>. 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<sup>6</sup>.

The British Thyroid Association's 'Guidelines for the management of thyroid cancer' (2014) 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 through the cancer drug fund for metastatic or

inoperable papillary and follicular thyroid cancer, which is refractory to radioiodine.

### The technologies

Lenvatinib (Lenvima, Eisai) inhibits multiple receptor tyrosine kinases including vascular endothelial growth factor (VEGF) receptors 1-3, fibroblast growth factor receptors 1-4, platelet-derived growth factor (PDGF) receptor alpha, stem cell growth factor receptor (SCFR), and Rearranged during Transfection. Lenvatinib is given orally and has a marketing authorisation in the UK for the treatment of adults with progressive, locally advanced or metastatic, differentiated (papillary/follicular/Hürthle cell) thyroid carcinoma, refractory to radioactive iodine.

Sorafenib (Nexavar, Bayer HealthCare) inhibits multiple receptor tyrosine kinases including VEGF receptors 2-3, PDGF receptor beta, FMS-like tyrosine kinase 3 and SCFR. 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.

<b>Intervention(s)</b>	<ul style="list-style-type: none"> <li>• Lenvatinib</li> <li>• Sorafenib</li> </ul>
<b>Population(s)</b>	Adults with progressive, locally advanced or metastatic, differentiated thyroid carcinoma, refractory to radioactive iodine.
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• The interventions listed above will be compared with each other</li> <li>• Best supportive care</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rate</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>The reference case stipulates that the time horizon for</p>

	<p>estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p>
<b>Other considerations</b>	<p>If the evidence allows, consideration will be given to subgroups based on previous treatment with tyrosine kinase inhibitors.</p> <p>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.</p>
<b>Related NICE recommendations and NICE Pathways</b>	<p><b>Related Technology Appraisals:</b></p> <p>Appraisals in development</p> <p>'Cabozantinib and vandetanib for treating unresectable locally advanced or metastatic medullary thyroid cancer'. NICE technology appraisals guidance [ID56]. Publication expected January 2018.</p> <p><b>Related Quality Standards:</b></p> <p>'Head and neck cancer'. NICE quality standard in development. Publication expected February 2017.</p> <p><b>Related NICE Pathways:</b></p> <p><a href="#">Head and neck cancer NICE pathway</a></p>
<b>Related National Policy</b>	<p><b>NHS England</b></p> <p>NHS England (2016) <a href="#">Manual for prescribed specialised services 13/14</a>. Specialist cancer services (adults) 105 (page 228)</p> <p>NHS England. <a href="#">National Programmes of care and clinical reference groups</a>. B16. Complex Head &amp; Neck (accessed August 2015)</p> <p><b>National Service Frameworks</b></p> <p><a href="#">Cancer</a></p> <p><b>Other policies</b></p> <p>Department of Health, NHS Outcomes Framework 2015-2016, Dec 2014. Domains 2, 4 and 5. <a href="https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf">https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385749/NHS_Outcomes_Framework.pdf</a></p>

### References

1. Guidelines for the management of thyroid cancer. Third edition. British Thyroid Association. February 2014.
2. Guidelines for the management of thyroid cancer. Third edition. British Thyroid Association. February 2014.
3. Thyroid cancer incidence. Cancer Research UK [accessed August 2016]
4. Types of thyroid cancer. NHS choices [accessed August 2016]
5. Types of thyroid cancer. Cancer Research UK [accessed August 2016]
6. Guidelines for the management of thyroid cancer. Third edition. British Thyroid Association. February 2014.