Scottish Medicines Consortium
Providing advice about the status of all newly licensed medicines
www.scottishmedicines.org.uk
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cabozantinib 20mg and 80mg hard capsules (Cometriq®) SMC No. (1022/15)

Swedish Orphan Biovitrum Ltd.

06 February 2015

The Scottish Medicines Consortium (SMC) has completed its assessment of the above product and advises NHS Boards and Area Drug and Therapeutic Committees (ADTCs) on its use in NHS Scotland. The advice is summarised as follows:

ADVICE: following a full submission considered under the ultra-orphan medicine process

cabozantinib (Cometriq®) is not recommended for use within NHS Scotland.

Indication under review: for the treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma.

In one pivotal, phase III study, cabozantinib was associated with a significant advantage in progression-free survival over placebo. However, the difference between cabozantinib and placebo did not reach statistical significance in the subgroup of patients with Rearranged during Transfection (RET) negative tumours. The summary of product characteristics therefore notes that for patients in whom RET mutation status is unknown or is negative, a possible lower benefit should be taken into account before individual treatment decision.

The submitting company did not present a sufficiently robust economic analysis and in addition their justification of the treatment's cost in relation to its benefits was not sufficient to gain acceptance by SMC.

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Overleaf is the detailed advice on this product.

Advice must be treated in strict confidence until published on the SMC website (www.scottishmedicines.org.uk) on **09 March 2015.**

Vice Chairman,
Scottish Medicines Consortium

Published 09 March 2015

Indication

For the treatment of adult patients with progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma. For patients in whom Rearranged during Transfection (RET) mutation status is unknown or is negative, a possible lower benefit should be taken into account before individual treatment decision.

Dosing Information

140mg orally once daily, taken as one 80mg capsule and three 20mg capsules. Treatment should be continued until the patient is no longer clinically benefitting from therapy or until unacceptable toxicity occurs. It should be expected that a majority of patients treated with cabozantinib will require one or more dose adjustments (reduction and/or interruption) due to toxicity. Patients should therefore be closely monitored during the first 8 weeks of therapy.

Therapy should be initiated by a physician experienced in the administration of anticancer medicinal products.

Product availability date

September 2014.
Cabozantinib meets SMC ultra-orphan criteria.

Summary of evidence on comparative efficacy

Medullary thyroid cancer is rare and accounts for approximately 3% of all thyroid cancers in adults. Approximately 75% are classified as sporadic and 25% as hereditary cancer syndrome with a well-characterized germline RET mutation. Patients are initially treated surgically and systemic chemotherapy and radiotherapy are not considered useful for most patients with medullary thyroid cancer (MTC). Metastatic disease is not curable, but since it can be quite indolent, patients are often monitored with scans and biochemical markers, with great variability in the timing of initiation of subsequent therapy. Targeted therapies (cabozantinib and vandetanib) are the treatment of choice for inoperable progressive and symptomatic disease.[1,2] Cabozantinib is a small molecule which inhibits multiple receptor tyrosine kinases (RET, MET [hepatocyte growth factor receptor protein] and vascular endothelial growth factor [VEGF] receptors) involved in tumour growth, angiogenesis, pathologic bone remodelling and metastatic progression of cancer.[3]

The evidence to support the use of cabozantinib in medullary thyroid cancer comes from the results of one pivotal, randomised, double-blind, phase III study (EXAM). Eligible patients were aged ≥18 years and had histologically confirmed, unresectable, locally advanced or metastatic medullary thyroid cancer with radiographic disease progression according to modified Response Evaluation Criteria in Solid Tumors (RECIST) criteria at screening compared to an image taken within previous 14 months. They also had an Eastern Co-operative Oncology Group (ECOG) performance status ≤2. Patients were randomised, in a ratio of 2:1, to receive cabozantinib (140mg orally once daily) or placebo (orally once daily) until disease progression according to mRECIST criteria or intolerable toxicity. Randomisation was stratified by age (≤65 years or >65 years) and prior treatment with a tyrosine kinase inhibitor (yes or no). Dose interruptions and dose reduction (to a minimum of 60mg daily) were permitted. On disease progression, patients were allowed to switch to alternative anticancer treatment but patients in the placebo group were not allowed to cross-over to receive cabozantinib.[4,5]

The primary outcome was progression-free survival (PFS), defined as the time from randomisation to progressive disease according to mRECIST criteria or death whichever occurred first. PFS was determined by an independent radiology review committee (IRC). At the cut-off April 2011 (after a median duration of follow-up of 13.9 months and a median duration of treatment of 204 days in the cabozantinib group and 105 days in the placebo group) a PFS event had occurred in 36% (79/219) of cabozantinib patients and 54% (60/111) of placebo patients. This included radiographic progression in 26% (58/219) and 45% (50/111) of patients and death in 9.6% (21/219) and 9.0% (10/111) of patients respectively. At the time of this analysis, the median PFS was 11.2 months (48.6 weeks) in the cabozantinib group and 4.0 months (17.4 weeks) in the placebo group: HR 0.28 (95% confidence interval [CI]: 0.19 to 0.40), <0.0001. At the time of this analysis, 64% (140/219) cabozantinib and 46% (51/111) placebo patients were censored but results of sensitivity analyses, performed to test the robustness of the results and to minimise the effect of potential informative censoring, were consistent with the primary analysis.[5] Pre-specified subgroup analyses found that the treatment effect in terms of PFS was consistent in all subgroups with all HR<1. However the difference did not reach statistical significance in the following, smaller subgroups: RET negative tumours, of non-white race and from centres in the rest of the world (not Europe or North America).[4,5]

Secondary outcomes included objective response rate, disease stabilisation and overall survival. Objective response rate (defined as the proportion of patients who had measurable disease at baseline for whom best objective response was complete or partial response according to mRECIST criteria, and which was confirmed by a subsequent visit ≥28 days later) was achieved by 28% (58/204) of cabozantinib patients and 0% (0/104) of placebo patients with measurable disease at baseline (p<0.0001). All responses in the cabozantinib group were partial and were achieved in RET positive (32%) and RET negative (25%) patients. [4,5]

Disease stabilisation (defined as the proportion of patients with measurable disease achieving a best objective response of confirmed complete or partial response or stable disease on or after week 24 without prior progressive disease or receiving subsequent therapy) was achieved by 55% (115/208) of cabozantinib patients and 13% (14/104) of placebo patients (p<0.0001). [4,5]

A planned interim analysis of overall survival was performed at the time of the primary PFS analysis and was based on 44% (96/217) deaths required for final analysis. This found no significant difference between the treatment groups: median overall survival was 21 months in the cabozantinib and not estimable in the placebo group: HR 0.98 (95% CI: 0.63 to 1.52). Death had been reported in 30% of cabozantinib and 27% of placebo patients.[4,5] An updated, but not pre-specified, overall survival analysis (cut-off date June 2012) was reported after 75% (162/217) of deaths required for the final analysis. The difference between groups was not significant: median overall survival was 26.0 months versus 20.3 months respectively: HR 0.83 (95% CI: 0.60 to 1.14). [3,5] Results of final overall survival analysis are awaited.

An exploratory outcome was the patient reported outcome MD Anderson Symptom Inventory Thyroid Cancer Module (MDASI THY) which assessed the severity of multiple thyroid cancer-related symptoms and the impact of these symptoms on daily functioning. It was performed at screening and every 12 weeks from randomisation until disease progression but completion beyond 24 weeks was low. At week 12, nausea, lack of appetite, dry mouth and feeling cold and at week 24, nausea, feeling cold and diarrhoea were clinically-meaningfully more severe in the cabozantinib compared to the placebo group. Only shortness of breath was more severe in the placebo group. Interference with quality of life was worse in both groups over time but was similar in both treatment groups at week 24.[5]

*Other data were also assessed but remain commercially confidential.**

Summary of evidence on comparative safety

No comparative safety data are available. Refer to the summary of product characteristics for details.

The European Medicines Agency (EMA) commented in the European Public Assessment Report (EPAR) that overall, the safety profile of cabozantinib was typical for a small molecule with targeted inhibition of the VEGF receptor and other tyrosine kinase-mediated pathways with hypertension, hand-foot syndrome, rash and gastrointestinal toxicities including diarrhoea, mucositis, fistulas, abscesses prominent, but haematologic toxicities limited.[5]

Summary of clinical effectiveness issues

Cabozantinib is the second medicine to receive a marketing authorisation for the treatment of medullary thyroid cancer. Vandetanib was the first but was not recommended for use by SMC on the basis of non submission. Current clinical guidelines recommend the use of targeted therapy (cabozantinib or vandetanib) for treatment of inoperable progressive and symptomatic disease. Clinical experts consulted by SMC considered that there is unmet need in this therapeutic area, namely that there are no medicines recommended for use by SMC. Cabozantinib meets SMC ultra-orphan criteria.

The key evidence from the pivotal study demonstrated a significant PFS advantage over placebo and the difference of 7.2 months was considered clinically relevant. PFS was based on radiological tumour assessment, performed every 12 weeks after randomisation until disease progression or death. Although subgroup analyses found that the treatment effect was consistent in all subgroups, the difference between cabozantinib and placebo did not reach statistical significance in the subgroups with RET negative tumours, of non-white race and from centres in the rest of the world (not Europe or North America).[4,5] The summary of product characteristics (SPC) therefore notes that for patients in whom RET mutation status is unknown or is negative, a possible lower benefit should be taken into account before individual treatment decision.[3]

Overall survival was a secondary outcome and current interim overall survival results suggest no survival benefit over placebo. Results of final survival analysis are awaited but data will be confounded by subsequent treatments received by patients on disease progression (33% of cabozantinib and 52% of placebo patients at June 2012 cut-off). Although the SPC notes that a relationship between prolonged PFS and significant improvement in overall survival has been demonstrated in the subgroup of RET M918T mutation positive patients, these results are based on post hoc, subgroup, interim analysis and should be treated with caution.[3]

There were a number of characteristics of the study population which may not fully represent the patients with medullary thyroid cancer in clinical practice including less than 5% of patients having locally advanced disease and the majority of patients were <65 years old. Also, eligible patients had radiographic progression within the previous 14 months.[5]

During the study, 79% (169/214) of cabozantinib and 9.2% (10/109) of placebo patients required a dose reduction of study drug and 65% (140/214) and 17% (19/109) respectively a dose interruption. Discontinuation due to adverse events were reported in 16% (35/219) of cabozantinib and 8.1% (9/111) of placebo patients.[4] Due to the indolent nature of advanced medullary thyroid cancer, the decision on when to initiate treatment is likely to be made on individual patient basis with the potential PFS benefits being balanced against a potential detrimental effect on quality of life from increased risk

of several cancer related symptoms, particularly gastrointestinal symptoms possibly related to the toxicity of the drug.[5] In patients aged ≥75 years, there was an increased rate of serious adverse events compared with patients <75 years (62% versus 40%).[5]

The introduction of cabozantinib would offer patients a licensed treatment option for locally advanced or metastatic medullary thyroid cancer as the only other licensed medicine, vandetanib, has not been recommended for use in NHS Scotland. There are no directly comparative data with vandetanib and, although an in-house indirect comparison exists, it was not evaluated since vandetanib was not considered a relevant comparator. In addition, there are differences between the pivotal studies for cabozantinib and vandetanib and in the latter study; patients were not required to have evidence of disease progression.[5] Clinical experts consulted by SMC considered that cabozantinib is a therapeutic advancement due to offering an effective treatment for improving PFS and that the place in therapy of cabozantinib would be in patients with rapidly progressive disease.

Cabozantinib has been authorised under a conditional approval scheme and further evidence on this medicinal product is awaited. The EMA will review new information on this medicinal product at least every year and the SPC will be updated as necessary.[3] The EPAR notes that based on efficacy data alone, it is not clear whether a lower dose than the maximum tolerated dose could be equally effective. The EMA considered that an additional dose-comparison study of cabozantinib 140mg daily versus 60mg daily is required in patients with hereditary or sporadic medullary thyroid cancer to address missing efficacy data.[5]

Summary of patient and clinician engagement

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of cabozantinib, as an ultra-orphan medicine, in the context of treatments currently available in NHS Scotland, specifically in the treatment of progressive, unresectable locally advanced or metastatic medullary thyroid cancer.

The key points expressed by the group were:

- Medullary thyroid cancer (MTC) can have a variable clinical course, ranging from indolent to rapidly progressive disease. Calcitonin over-production in metastatic disease frequently causes terrible intractable diarrhoea. Other symptoms such as weight loss, neck pain and chronic fatigue can mean patients are unable to work and are very dependent on carers.

- Once surgery is exhausted as an option, there are no currently approved active treatments for MTC. PACE participants described metastatic MTC as a chemo resistant disease. Cabozantinib is a huge improvement on standard chemotherapy options. The intractable diarrhoea and pain are particularly burdensome symptoms and relief from these greatly enhances quality of life. Cabozantinib has a different side effect profile to other TKI's which can be advantageous.

- PACE participants highlighted that cabozantinib enables patients to contribute to family life and regain a near normal life-style. The ability to return to work has economic benefits for the wider family. The company's proposed positioning for cabozantinib was supported. Patients with intractable hormonal symptoms and clearly progressive disease would benefit.

- PACE participants expressed strong support for the availability of cabozantinib in Scotland. It can provide real benefits to patients with progressive MTC in whom there are no other options.

Summary of ultra orphan decision-making framework

Cabozantinib has been considered by SMC using its decision-making framework for the assessment of ultra-orphan medicines. Relevant factors under each of the criteria are summarised below:

Nature of the condition
Medullary thyroid cancer is a rare cancer with a disproportionately large impact because of the high rate of metastases and lack of currently approved active treatments. Hormone over-production in metastatic disease frequently causes terrible intractable diarrhoea which has a significant detrimental impact on quality of life. The disease can have a variable clinical course ranging from indolent to rapidly progressive with symptoms such as weight loss, coughing, neck pain and chronic fatigue. Patients may also suffer depression. As such, quality of life in patients can be significantly affected.

Impact of the new technology
Once surgery is exhausted as an option, there is currently no approved active treatment for progressive, unresectable locally advanced or metastatic medullary thyroid carcinoma. Standard chemotherapy may be offered but is considered little better than best supportive care. Radiotherapy is sometimes used for local disease. Cabozantinib is therefore seen as an advance on standard chemotherapy options.

The evidence supporting the use of cabozantinib comes from a randomised, double-blind phase III study. The results of this study demonstrated a significant PFS advantage over placebo and the difference of 7.2 months was considered clinically relevant. Final overall survival data are not yet available from this study but the economic modelling undertaken by the company predicted a survival gain of 10.8 months.

The side-effects reported with cabozantinib treatment include hypertension, hand-foot syndrome, rash and gastrointestinal toxicities including diarrhea, mucositis, fistulas, and abscesses prominent.

Value for money
The submitting company presented a cost-utility analysis of cabozantinib compared to best supportive care (BSC) in patients with progressive, unresectable locally advanced or metastatic MTC. A 3 state Markov model (non-progressed, progressed and death) was used with a lifetime time horizon. Vandetanib was not included as a comparator on the grounds that it is not recommended by SMC (due to non-submission).

The clinical data used were from the EXAM study, with the placebo arm used as a proxy for BSC. Time to progression and overall survival were extrapolated by fitting best fitting parametric functions to the observed data. Patients who switched treatments after study drug discontinuation were censored in the economic analysis. In addition, an analysis was performed for the sub-group of patients in the EXAM study who were RET mutation positive.

Base case utility estimates for the non-progressed and progressed disease states (0.796 and 0.624 respectively) were derived from published trial data in thyroid cancer in which SF36 outcomes had been converted to utilities by mapping to EQ- 5D and converting to SF-6D values for the non-progressed and progressed states respectively. Disutilities derived from published sources were applied to a number of treatment-related adverse events.

Cabozantinib drug acquisition costs were the same for each dose patients received over the course of treatment based on the EXAM trial. No drug costs were included for the BSC comparator, and no

post-progression drug therapy costs were included. Costs for monitoring (consisting of electrolyte testing for cabozantinib every 3 months), adverse event management, and MTC management costs for the non-progressed and progressed health states were included. The latter was assumed to consist of a consultant/multi-disciplinary team visit every 6 months in the non-progressed state, and every 10 days in the progressed state, with these estimates based on expert opinion. An end of life cost in the last month has also been included.

The incremental cost-effectiveness ratio (ICER) for cabozantinib vs. BSC was estimated to be £93,141 per quality-adjusted life-year (QALY) gained, based on incremental cost of £66,204, incremental life years gained of 0.90 (or 10.8 months) and incremental QALYs of 0.71. The cost difference was driven by the additional drug costs for cabozantinib. Scenario analysis performed demonstrated sensitivity to increasing cabozantinib cost (a 30% increase increased the ICER to £121k/QALY, although this does not account for any potential impact on life year and QALY outcomes), and sensitivity to the health state utility estimates with lower utilities of 0.624 and 0.52 assumed for the non-progressed and progressed health states respectively resulting in an increased ICER of £117k/QALY.

There were a number of limitations with the economic analysis:

- The data on overall survival that were used in the economic model were not mature and not statistically significant versus placebo. The estimates of survival benefit in the sub-group with RET +ve status were based on a post-hoc, interim analysis and hence are uncertain. Other limitations with the clinical evidence have been noted in the clinical effectiveness section.
- Additional sensitivity analyses requested from the company demonstrated high sensitivity to varying the projected overall survival estimate by the lower and upper 95% confidence interval (CI) for cabozantinib, with an ICER range of £49k - £692k/QALY. A subgroup analysis of patients with RET +ve mutation status was also provided and the ICER for this group was also sensitive to varying the projected OS estimates by the 95% CIs, with an ICER range of £34k - £143k/QALY. However, using an alternative parametric function for OS reduced the ICERs. As the difference in OS from the EXAM trial for cabozantinib versus placebo in all patients was not statistically significant, assuming no difference in OS in the model increased the ICER to £700k.
- The base case utility estimates, in particular for the non-progressed health state, are likely to be overestimated as they are based on studies containing patients with stage 1 and 2 thyroid cancer and so with less severe disease than those eligible for cabozantinib. In addition, the highest thyroid cancer utility estimates for the non-progressed state and lowest value for the progressed state have been selected of those available. A scenario applying a 10% lower utility value for the non-progressed state increases the ICER to £100k/QALY.
- The estimates of resource use in each health state are over-simplistic and lack sufficient breadth of resource coverage. Based on SMC clinical expert feedback the estimates that are provided for consultant visits are underestimated for the non-progressed state, and likely to be overestimated for the progressed state. The costs associated with adverse management and monitoring may also be underestimated. However, the impact of these biases on the ICER is unlikely to be large.
- The economic analysis was potentially further oversimplified by not taking account of treatments that may be received after cabozantinib and by assuming no drug treatment was received in the BSC arm pre or post progression. The impact this may have on the ICER is unclear.

Patient and Clinician Engagement
A Patient and Clinician Engagement (PACE) meeting was held for this submission. Participants at the meeting indicated a range of potential impacts of the new technology for the patient and families/ carers.

Impact beyond direct health benefits and on specialist services
At the PACE meeting, participants felt that cabozatanib offered real benefits to the small group of patients with progressive disease when there were no other treatment options. Participants indicated that the treatment could allow patients to return to work and be less reliant on family and carers given the improved quality of life on treatment. It was reported that treatment could improve energy levels, and by allowing patients to lead a near normal lifestyle, could improve self-esteem.

Costs to the NHS and Personal Social Services
The submitting company has estimated that 3 patients would be treated with cabozatanib each year and that this would be associated with a medicines budget impact of £156k. The submitting company did not estimate any costs outside of the NHS.

The Committee also considered the benefits of cabozantinib in the context of the SMC decision modifiers and agreed that the criterion for the absence of other treatments of proven benefit was met. In addition, as cabozantinib is an ultra-orphan medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, and after application of the appropriate SMC modifiers, the Committee was unable to accept cabozantinib for use in NHS Scotland.

*Other data were also assessed but remain commercially confidential.**

Summary of patient and public involvement

The following information reflects the views of the specified Patient Groups.

- Submissions were received from the British Thyroid Foundation (BTF) and the Association for Multiple Endocrine Neoplasia Disorders (AMEND), which are both registered charities.
- Both charities have received pharmaceutical company funding in the past two years, but not from the submitting company.
- Metastatic medullary thyroid cancer (MTC) is a rare type of thyroid cancer. There is no cure.
- Metastatic MTC is a rare condition that impacts severely on the quality of life of patients and their families. Patients cope with many debilitating physical symptoms, particularly chronic diarrhoea and fatigue. The severity of the symptoms causes patients to be unable to work and family may also have to give up work to care for them. This causes additional stress and hard-ship. There is currently no other treatment options for these patients.
- Cabozantinib offers patients the potential for an extended period of progression-free survival and potentially improved quality of life. Cabozantinib is easily taken in tablet form, and whilst there are some side-effects such as rash, nausea and hand and foot sores, treatment holidays and support can help with these.

Additional information: guidelines and protocols

The British Thyroid Association published "Guidelines for the management of thyroid cancer" in 2014.[1] These recommend that patients with confirmed medullary thyroid cancer should undergo RET mutation analysis to investigate potential genetic heritability. The guidelines outline surgery is the key treatment for medullary thyroid cancer that may in some cases provide a biochemical and clinical cure. As a minimum, patients should undergo total thyroidectomy and central compartment node dissection, however the extent of surgery will be based on variables including RET analysis, measurements of calcitonin, metastases and tumour size. Following surgery patients should be given thyroxine. The guidelines report that external beam radiation therapy (EBRT) should only be considered after surgery and where there is a significant risk of local recurrence. For inoperable progressive and symptomatic disease, targeted therapies are the treatment of choice. Vandetanib and cabozantinib have both been shown to provide progression free survival over placebo in randomized controlled trials, although neither has been found to improve survival.

The European Society for Medical Oncology (ESMO) published "Thyroid cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up", in 2012.[6] These recommend that all patients should undergo a biochemical preoperative evaluation to identify characteristics of the disease such as severity, comorbid conditions and phaeochromocytoma. In patients with no evidence of lymph node metastases, the recommended treatment is total thyroidectomy followed by replacement thyroxine. In cases of distant metastases, unifocal and/or small tumors, this may not be appropriate and less extensive surgery can be considered. In cases of distant metastasis the guidelines report mono or polychemotherapy has not been found to have any significant clinical benefit, with radiotherapy used for local invasion of cancer and chemoembolization used in the treatment of liver metastases. The guidelines report on the clinical benefits of new compounds such as targeted kinase inhibitors including vandetanib which they note is now approved by the EMA and FDA [Food and Drug Administration] in the treatment of patients with locally advanced metastatic medullary thyroid cancer. This guideline predates the availability of cabozantinib.

The European Thyroid Association published "Guidelines for metastatic medullary thyroid cancer" in 2012.[7] These recommend considering treatment based on disease severity, disease recurrence and progression rate. Local treatment procedures targeting the predominant lesion(s) (with follow-up at regular intervals) are recommended for asymptomatic patients with low tumor burden and stable disease. Systemic treatment is recommended for patients showing symptoms, large tumor burden and progression on imaging. Specific recommendations are provided for metastases of the brain, bone, lung and liver. Treatment recommendations include surgery for isolated or few metastases, radiofrequency ablation, EBRT and chemoembolization. Systemic therapy using conventional cytotoxic chemotherapy drugs are not recommended for first-line therapy in patients with persistent or recurrent medullary thyroid cancer. Targeted therapies, using kinase inhibitors directed against RET and VEGF receptor are highlighted as the most effective treatment option, described as 'major progress' in the treatment of this disease. At the time of publication (2012) vandetanib and cabozantinib were entering phase III clinical trials and reported as showing high rates of disease control, with improvements in quality of life and significant improvement in progression-free survival.

Additional information: comparators

The only other medicine licensed for use for medullary thyroid cancer is vandetanib which has not been recommended for use in NHS Scotland by SMC.

Cost of relevant comparators

Drug	Dose Regimen	Cost per 28 days (£)
Cabozantinib	**140mg orally daily**	**4,800**
Vandetanib*	300mg orally daily	4,667

*vandetanib was not recommended for use in NHS Scotland by SMC. Doses are for general comparison and do not imply therapeutic equivalence. Treatment for both medicines is continued until the patient is no longer benefiting from treatment but is presented above for 28 days to allow general comparison. Costs for cabozantinib from eMIMS 6 November 2014 and costs for vandetanib from eVadis and eMIMS on 6 November 2014.

Additional information: budget impact

The submitting company estimated there to be 5 patients each year eligible for treatment with cabonzantinib with an estimated uptake rate of ~50% (3 patients) each year. The submitting company estimated the medicines budget impact to be £156k per year, with no displacement of other drugs.

References

The undernoted references were supplied with the submission. Those shaded in grey are additional to those supplied with the submission.

1. Perros P, Colley S, Boelaert K et al. British Thyroid Association Guidelines for the Management of Thyroid Cancer. Clinical Endrocrinology 2014;81 (Supplement 1):1-122.

2. Haddad RI. How to incorporate new tyrosine kinase inhibitors in the treatment of patients with medullary thyroid cancer. Editorial. J Clin Oncology 2013;31:3618-20.

3. Swedish Orphan Biovitrum Ltd. Cometriq hard capsules summary of product characteristics, 17 September 2014. [accessed 7 October 2014]

4. Elisei R, Schlumberger M, Muller SP et al. Cabozantinib in progressive medullary thyroid cancer. J Clin Oncol 2013;31:3639-46

5. European Medicines Agency. Public Assessment Report: cabozantinib, procedure number EMEA/H/C/002640/0000. www.ema.europa.eu [accessed 7 October 2014]

6. Pacini F, Castagna MG, Brilli L et al. Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Annals of Oncology 2012;23 (Supplement 7):vii10-vii19.

7. Schlumberger M, Bastholt L, Dralle H et al. 2012 European Thyroid Association Guidelines for Metastatic Medullary Thyroid Cancer. European Thyroid Journal 2012;1:5-14.

This assessment is based on data submitted by the applicant company up to and including 10 December 2014.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal: http://www.scottishmedicines.org.uk/About_SMC/Policy_Statements/Policy_Statements*

Drug prices are those available at the time the papers were issued to SMC for consideration. SMC is aware that for some hospital-only products national or local contracts may be in place for comparator products that can significantly reduce the acquisition cost to Health Boards. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document. Area Drug and Therapeutics Committees and NHS Boards are therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Advice context:

No part of this advice may be used without the whole of the advice being quoted in full.

This advice represents the view of the Scottish Medicines Consortium and was arrived at after careful consideration and evaluation of the available evidence. It is provided to inform the considerations of Area Drug & Therapeutics Committees and NHS Boards in Scotland in determining medicines for local use or local formulary inclusion. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.