

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Draft guidance consultation

Cabozantinib for previously treated advanced differentiated thyroid cancer unsuitable for or refractory to radioactive iodine

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using cabozantinib in the NHS in England. The evaluation committee has considered the evidence submitted by the company and the views of non-company stakeholders, clinical experts and patient experts.

This document has been prepared for consultation with the stakeholders. It summarises the evidence and views that have been considered, and sets out the recommendations made by the committee. NICE invites comments from the stakeholders for this evaluation and the public. This document should be read along with the evidence (see the [committee papers](#)).

The evaluation committee is interested in receiving comments on the following:

- Has all of the relevant evidence been taken into account?
- Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?
- Are the recommendations sound and a suitable basis for guidance to the NHS?
- Are there any aspects of the recommendations that need particular consideration to ensure we avoid unlawful discrimination against any group of people on the grounds of age, disability, gender reassignment, pregnancy and maternity, race, religion or belief, sex or sexual orientation?

Note that this document is not NICE's final guidance on this technology. The recommendations in section 1 may change after consultation.

After consultation:

- The evaluation committee will meet again to consider the evidence, this evaluation consultation document and comments from the stakeholders.
- At that meeting, the committee will also consider comments made by people who are not stakeholders.
- After considering these comments, the committee will prepare the final draft guidance.
- Subject to any appeal by stakeholders, the final draft guidance may be used as the basis for NICE's guidance on using cabozantinib in the NHS in England.

For further details, see [NICE's manual on health technology evaluation](#).

The key dates for this evaluation are:

- Closing date for comments: 28 April 2023
- Second evaluation committee meeting: 11 May 2023
- Details of membership of the evaluation committee are given in section 4

1 Recommendations

- 1.1 Cabozantinib is not recommended, within its marketing authorisation, for treating locally advanced or metastatic differentiated thyroid cancer (DTC) that is unsuitable for or refractory to radioactive iodine, and that has progressed after systemic treatment, in adults.
- 1.2 This recommendation is not intended to affect treatment with cabozantinib that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Why the committee made these recommendations

Standard treatment for advanced DTC that is unsuitable for, or does not respond (refractory) to, radioactive iodine, and that has got worse after systemic treatment, is best supportive care.

Clinical trial evidence shows that, compared with best supportive care, cabozantinib increases how long people have before their condition gets worse. But it is not clear if it increases how long people live. This is because people were not followed up for long enough, and because of how the trial was done.

Because it is not clear if cabozantinib increases how long people live, the most likely cost-effectiveness estimates are not clear. Because of this, they would need to be towards the lower end of the range that NICE considers an acceptable use of NHS resources. But the most likely cost-effectiveness estimates are towards the higher end of the range that NICE considers an acceptable use of NHS resources. This is true even when considering the condition's severity, and its effect on quality and length of life.

More evidence could help address the uncertainty about the benefits of cabozantinib, but the company said that there would be no more evidence from the trial. So, cabozantinib is not recommended.

2 Information about cabozantinib

Marketing authorisation indication

- 2.1 Cabozantinib (Cabometyx, Ipsen) is indicated 'as monotherapy for the treatment of adult patients with locally advanced or metastatic differentiated thyroid carcinoma (DTC), refractory or not eligible to radioactive iodine (RAI) who have progressed during or after prior systemic therapy'.

Dosage in the marketing authorisation

- 2.2 The dosage schedule is available in the [summary of product characteristics for cabozantinib](#).

Price

- 2.3 The list price of cabozantinib is £5,143 for a 30-tablet pack of 20 mg, 40 mg or 60 mg tablets (excluding VAT; BNF online accessed March 2023).
- 2.4 The company has a commercial arrangement. This makes cabozantinib available to the NHS with a discount and it would have also applied to this indication if the technology had been recommended. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

3 Committee discussion

The [evaluation committee](#) considered evidence submitted by Ipsen, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

Clinical management

Clinical need

- 3.1 Differentiated thyroid cancer (DTC) is the most common form of thyroid cancer, accounting for around 90% to 95% of all diagnosed cases. More women than men are diagnosed with the condition. But the proportions of men and women are similar for people with metastatic disease. Treatment typically involves surgery, usually with the aim of curing the condition. This means that radioactive iodine may be used after surgery, to destroy any cancerous cells not removed by surgery and those that have spread beyond the thyroid. Radioactive iodine is an intensive intervention. But between 5% and 15% of patients have DTC that is refractory to radioactive iodine. The clinical expert described previously treated locally advanced or metastatic DTC unsuitable for or refractory to radioactive iodine as a severe condition with a heavy symptom burden. Bone metastases can affect mobility, and prognosis is usually poor. For radioactive iodine-refractory locally advanced or metastatic DTC, NICE recommends first-line treatment with lenvatinib or sorafenib (see [NICE's technology appraisal guidance on lenvatinib and sorafenib](#)). But there are no NICE-recommended second-line treatments for people whose condition progresses on first-line treatment. The committee recognised that there is an unmet need for people with previously treated locally advanced or metastatic DTC that is unsuitable for or refractory to radioactive iodine.

Treatment options

- 3.2 For people whose condition has progressed on lenvatinib or sorafenib, and who are no longer having treatment with them, the only remaining option is best supportive care. This typically includes thyroid stimulating hormone suppression with an appropriate thyroid hormone treatment, and ongoing imaging, with palliative radiotherapy and symptom relief when necessary. NICE recommends selpercatinib for treating advanced RET (rearranged during transfection) fusion-positive thyroid cancer (see

[NICE's technology appraisal guidance on selpercatinib](#)). NICE recommends entrectinib and larotrectinib for treating NTRK (neurotrophic tyrosine receptor kinase) fusion-positive solid tumours (see [NICE's technology appraisal guidance on entrectinib](#) and [larotrectinib](#)). DTC can be NTRK fusion positive. Selpercatinib, entrectinib and larotrectinib are all recommended for use in the Cancer Drugs Fund (CDF) and are not part of routine NHS commissioning. Also, these drugs are only used if DNA analysis of the tumours identifies specific changes in the RET and NTRK genes, and these changes are uncommon in radioactive iodine-refractory locally advanced or metastatic DTC. The company selected best supportive care as the only comparator for cabozantinib. It said that there are no other routinely commissioned treatments recommended by NICE after first-line systemic treatment of radioactive iodine-refractory DTC. It also explained that lenvatinib and sorafenib can only be used at first line in clinical practice, and selpercatinib is only recommended in the CDF. This was confirmed by the clinical experts. [NICE's health technology evaluations manual](#) says that technologies that have been recommended by NICE with managed access (for example, in the CDF) are not considered established practice in the NHS and are not considered suitable comparators. The EAG noted that some clinicians may continue to offer lenvatinib after progression. But the company did not include continued lenvatinib used after progression in its economic model. Neither was lenvatinib listed as a comparator in the final NICE scope. The EAG also recognised that there was unlikely to be enough evidence for a reliable comparison between cabozantinib and continued lenvatinib used post-progression. The clinical experts acknowledged that lenvatinib may be continued after progression in clinical practice, but that this would be in very specific situations. The clinical experts confirmed that best supportive care was the only appropriate comparator. The committee concluded that placebo plus best supportive care was the most appropriate comparator for cabozantinib plus best supportive care.

Positioning of cabozantinib

3.3 In the main clinical trial, COSMIC-311 (see [section 3.4](#)), approximately 76% of people had previously had either sorafenib or lenvatinib, and 24% had had both. The company proposed cabozantinib as a second-line treatment option for previously treated locally advanced or metastatic DTC unsuitable for or refractory to radioactive iodine. NHS England's Cancer Drugs Fund clinical lead confirmed that NHS England commissions only 1 of either lenvatinib or sorafenib for treating DTC after radioactive iodine. Lenvatinib is more frequently prescribed in clinical practice than sorafenib. The clinical expert agreed that people would not have both lenvatinib and sorafenib, unless they had had to stop taking either within 3 months of starting it because of toxicity. The marketing authorisation for cabozantinib included second-line or later-line treatment after prior systemic therapy (see [section 2.1](#)). The committee was also aware that there are no treatments recommended by NICE for after first-line systemic treatment of radioactive iodine-refractory DTC (see [section 3.2](#)). The committee concluded that the company's positioning of cabozantinib as a second-line treatment option was appropriate.

Clinical effectiveness

COSMIC-311 trial

3.4 The main evidence for cabozantinib came from COSMIC-311. This is a phase 3, randomised, double-blind, controlled study comparing cabozantinib plus best supportive care with placebo plus best supportive care. It included adults with radioactive iodine-refractory advanced DTC whose condition had progressed during or after previous systemic therapy. The primary endpoints were ORR and progression-free survival (PFS). COSMIC-311 reported 2 clinical cut-offs for data: the primary clinical cut-off (CCO1) in August 2020, and a secondary data cut-off (CCO2) in February 2021. CCO1 had a median follow up of 6.2 months, and CCO2 had a median follow up of 10.1 months, for the full intention-to-treat (ITT) population. PFS significantly improved for cabozantinib

compared with placebo in both data cuts. At CCO2 (n=258), the hazard ratio for PFS in the ITT population was 0.22 for cabozantinib compared with placebo (96% confidence interval [CI] 0.15 to 0.32, $p < 0.0001$). The EAG noted that a large proportion of patients had censored data (64% in the cabozantinib group and 22% in the placebo group at CCO2). So, there was a lot of incomplete information for PFS and overall survival (OS) in the CCO2 follow up. There was no statistically significant difference in OS between the 2 treatment arms in either data cut-off. At CCO2, the hazard ratio for OS was 0.76 for cabozantinib compared with placebo (95% CI 0.45 to 1.31, p value is confidential and cannot be reported here). The PFS and OS hazard ratios for cabozantinib compared with placebo in the second-line population were better than those estimated for the full ITT population. But the hazard ratios in the second-line population are confidential and cannot be reported here. The EAG was concerned that, because the second-line population was a subgroup of COSMIC-311, the sample size was smaller and there was greater uncertainty in the trial results. The EAG also cautioned that the integrity of the survival data was compromised by the large proportion of people having placebo who, on radiographic progression, had open-label cabozantinib (see [section 3.5](#)). The committee recognised that cabozantinib plus best supportive care showed a significant improvement in PFS compared with placebo plus best supportive care. But there was no statistically significant difference in OS. The clinical experts explained that it would be unusual for a PFS benefit not to translate into an OS benefit when there are limited treatment options available and there is otherwise a very poor prognosis. So, the clinical experts considered that it was likely that there would be an OS benefit for people treated with cabozantinib. But it was uncertain how much OS benefit there would be. The committee appreciated that the company had presented randomised controlled data collected in COSMIC-311. The committee also understood the limitations of the study and that by focusing on the relevant second-line population, it had

reduced the evaluable sample. But the committee can only consider the data presented. It acknowledged that the survival results were uncertain.

Crossover adjustment

3.5 The EAG assessed the risk of bias in the COSMIC-311 trial to be high because of deviations from the intended treatment. After radiographic progression, people having placebo could cross over, if eligible, to open-label cabozantinib. People having cabozantinib could also continue having open-label cabozantinib after radiographic progression if the investigator deemed that they were still getting clinical benefit. Large proportions of people in the placebo group switched treatment within a relatively short period from the start of the trial (31% at CCO1, and 45% at CCO2, in the ITT population). The company did crossover adjustment analyses on the OS data to estimate the unbiased survival benefit of cabozantinib treatment compared with the placebo arm. It explored 3 adjustment methods: rank-preserving structural failure time (RPSFT), two-stage estimation, and inverse-probability-of-censoring weightings. All 3 methods gave similar results. The company used the RPSFT method in its base case because it was in line with previous NICE submissions. The OS hazard ratio for cabozantinib compared with RPSFT-adjusted placebo in the ITT population was 0.65 (95% CI 0.28 to 1.53). The hazard ratio in the second-line population is confidential and cannot be reported here. But there was a non-statistically significant trend in improved OS for cabozantinib plus best supportive care compared with placebo plus best supportive care, with or without crossover adjustment. The committee understood that the OS results were confounded by the short time to progression in the placebo arm, combined with the high levels of censoring and crossover in COSMIC-311. It recognised the crossover adjustment methods explored by the company, and it was familiar with the uncertainty associated with them. The committee concluded that the OS

data was uncertain, even after the company adjusted for crossover, and concluded that it would take this into account during its decision making.

Economic model

Company's modelling approach

3.6 The company used a partitioned survival model with 3 health states: progression-free disease, progressed disease, and death, to model the cost effectiveness of cabozantinib plus best supportive care. The company base-case analysis used the second-line subgroup of COSMIC-311 at CCO2, including the RPSFT-adjusted data for placebo plus best supportive care (see [section 3.3](#) and [section 3.5](#)). The EAG considered the company's model to be generally in line with NICE's reference case. But the EAG noted that it deviated from the reference case. This was because it used utility values taken from a general population time-trade-off study in preference to the EQ-5D-5L data collected in COSMIC-311 and mapped to EQ-5D-3L (see [section 3.8](#)). The committee concluded that the company's second-line subgroup model was acceptable for decision making.

Modelling overall survival

3.7 The company fitted parametric survival models to the data for the second-line-only population in COSMIC-311. This informed the company's base-case analysis. It selected the PFS and OS distributions based on visual and statistical fit to the observed data. The company also used clinical experts' expectations of OS at 2, 5 and 10 years in people with radioactive iodine-refractory DTC having cabozantinib or best supportive care. The company noted that all OS curves overestimated the clinical experts' survival expectations at 5 and 10 years. The parametric survival distributions for PFS and OS selected by the company for the second-line base-case analysis were the Weibull and the exponential, respectively. The EAG had several concerns about the company's modelling of OS. It explained that the company's model assumes proportional hazards. But

the survival data from COSMIC-311 shows that the treatment effect for cabozantinib plus best supportive care compared with placebo plus best supportive care reduces over time. This is shown by the survival curves coming together, indicating that the proportional hazards assumption did not hold. The EAG also used exponential distributions to model OS for both cabozantinib plus best supportive care and placebo plus best supportive care in its preferred analysis. It noted that this gave the second most pessimistic survival curve for placebo plus best supportive care. The EAG explored applying a treatment benefit cap. This analysis used the exponential models of its preferred analysis and applied the OS hazard for best supportive care to both groups after 36 months. But the EAG cautioned that the 36-month timepoint at which the treatment benefit cap was applied was arbitrary. The EAG stressed that neither its analysis nor the company's analysis was ideal for modelling OS and that this was unresolvable given the limited and immature data available. The clinical experts noted that there was limited data from which to model OS, particularly in the placebo plus best supportive care group. It described how low patient numbers and short follow up from COSMIC-311 explained why attempts to model OS lacked clinical plausibility. The EAG considered that longer follow up in COSMIC-311 would help to reduce uncertainty in OS estimates. But the company explained that no further data cuts were planned from COSMIC-311. The committee agreed that longer follow-up data would be helpful for reducing uncertainty, but acknowledged that it was unlikely that this would become available in the future. The committee agreed that it was uncertain whether the OS models done by either the company or the EAG reflected the true long-term benefit of cabozantinib on OS. But the committee concluded that it preferred to use the exponential distribution for modelling OS in both treatment arms in its decision making.

Utility values

Source of utility values

3.8 The company's model used health-state utility values based on the adjusted regression model reported by Fordham et al. (2015). These values were a progression-free utility of 0.87, and a progressed-disease utility of 0.52. The EAG was concerned that the utility applied by the company in the progression-free state was higher than the age- and sex-matched EQ-5D-3L value for the general population. The general population utility was 0.82. At technical engagement, the company and the EAG agreed that an age-adjusted general population utility cap should be applied. This would ensure that health-related quality of life in the radioactive iodine-refractory DTC population could not exceed health-related quality of life in the general population. The clinical experts also agreed that it was not plausible that people with radioactive iodine-refractory DTC would have a higher utility value than the UK general population. The company's second-line base-case model had mistakenly removed a constraint. This constraint had been applied to prevent the utility value for the progression-free health state from exceeding the estimated EQ-5D-3L utility value for the age- and sex-matched general population. So, the EAG corrected the model. The EAG explained that some NICE technology appraisal guidance on treatments for thyroid cancer had also applied utility values from Fordham et al. (2015). These were [NICE's technology appraisal guidance on cabozantinib for medullary thyroid cancer](#), [vandetanib for medullary thyroid cancer](#) and [selpercatinib for advanced thyroid cancer with RET alterations](#). But, in each of these technology appraisals, EQ-5D data had not been collected in the pivotal clinical trials, and the unadjusted utility values from Fordham et al. (2015) were used. These were a progression-free utility of 0.80 and a post-progression utility of 0.50. The EAG used the unadjusted utility values in its preferred analysis, for consistency with the previous appraisals. The clinical experts explained that people having treatment at second line were expected to have a poorer prognosis and lower health-related quality

of life than at first line. So, they expected the utility for people at second line to be lower. But the Fordham et al. (2015) utility values based on the adjusted regression model were higher than the unadjusted utility values used in the previous NICE appraisals for thyroid cancer. The committee considered that it would be more appropriate to use the utility estimate from COSMIC-311 than Fordham et al. (2015). It noted that the [NICE health technology evaluations manual](#) says that health-related quality of life should be measured directly by patients. The manual also advises using the EQ-5D measurement method to measure health-related quality of life in adults. The EQ-5D-5L data from the COSMIC-311 trial was mapped to EQ-5D-3L using the crosswalk approach by Hernandez-Alava and Pudney (2017). The company noted that quality-of-life data collection stopped shortly after progression in COSMIC-311. It also noted that it preferred to use the same source for both the progression-free and the progressed-disease utility values. The EAG agreed it would be reasonable to consider the COSMIC-311 utility values. It recalled that it had explored using the COSMIC-311 utility value for the progression-free state with its preferred unadjusted post-progression utility from Fordham et al. (2015) in sensitivity analyses. The committee concluded that it preferred using the COSMIC-311 utility value for the progression-free state because it was based on the population being appraised and because it used the same source as that used for the model's clinical efficacy inputs. It also recognised that the EQ-5D-5L data available from COSMIC-311 for informing the progressed-disease utility was limited. So, it concluded that the unadjusted post-progression utility from Fordham et al. (2015) was preferred for decision making.

Costs

Post-progression cabozantinib costs

3.9 In COSMIC-311, 1.6% of people in the cabozantinib group had had post-progression open-label cabozantinib at CCO1 (see [section 3.5](#)). It was 6.5% at CCO2. The clinical experts considered it likely that, in clinical

practice, some people would continue on cabozantinib beyond radiological progression if they were still benefiting from treatment. This is in the absence of any other further lines of treatment. At technical engagement, the company agreed that the costs of post-progression cabozantinib should be included in the economic analysis. This would reflect the intention for cabozantinib to be used in line with its marketing authorisation. But the EAG was concerned that the company's selected model for time to treatment discontinuation (TTD), generalised gamma, remained lower than the modelled PFS function at all timepoints. This implied that people do not have post-progression cabozantinib. The EAG's preferred analysis used a Weibull model for TTD. But the EAG recognised that there were other functions that were equally plausible and that also gave TTD predictions that were above PFS. The Weibull was considered to be conservative compared with other alternatives. The committee understood that, in clinical practice, some people would continue on cabozantinib beyond radiological progression. So, the TTD curve should be above the PFS curve. It concluded that the EAG's Weibull model for TTD was appropriate for decision making.

Drug cost adjustments

3.10 In the company's base-case analysis, drug acquisition costs were adjusted based on relative dose intensity. This is the average amount of planned dose that the person had. The EAG considered it more appropriate to adjust cabozantinib costs based on adherence, given the flat pricing structure for cabozantinib. Adherence is the proportion of days on which patients had treatment. The company recalled that previous NICE technology appraisals had used relative dose intensity to adjust drug acquisition costs. This was regardless of whether the technology had a flat pricing structure across different dosage strengths. It also noted that the adherence estimate was based on CCO1, whereas a relative dose intensity estimate was available from CCO2. The committee acknowledged that the relative dose intensity approach aligned with methods used in previous technology appraisal guidance. But it concluded

that the EAG's adjustment based on adherence was more appropriate for decision making, because it reflected the true drug acquisition cost of cabozantinib to the NHS.

Severity

QALY weighting

3.11 In its submission, the company provided evidence that previously treated locally advanced or metastatic DTC unsuitable for or refractory to radioactive iodine is a severe condition. The committee considered the severity of the condition (the future health lost by people living with the condition and having standard care in the NHS). The committee may apply a greater weight (a severity modifier) to QALYs if technologies are indicated for conditions with a high degree of severity. The company provided absolute and proportional QALY shortfall estimates in line with [NICE's health technology evaluations manual](#). The company's evidence to inform the QALYs of people without the condition was based on the COSMIC-311 ITT population at CCO2. This population had a mean baseline age of 65 years, and 47% were men. The company's evidence for QALYs of people with the condition on best supportive care was based on its preferred utility values from Fordham et al. (2015). These were based on an adjusted regression analysis (see [section 3.8](#)). The committee noted that the company's absolute QALY shortfall calculation results were below 12. Their proportional QALY shortfall calculation results were between 0.85 and 0.95. (The exact figures are confidential and so cannot be reported here.) The committee is allowed to apply a greater weight to the QALYs for technologies indicated for conditions with a high degree of severity. The committee considered this advice on severity as a decision modifier. It noted that if either the absolute or the proportional QALY shortfall calculated falls on the cut-off between severity levels, the higher severity level will apply. The company said that the absolute QALY shortfall was less than 12, which would imply no QALY weight. But a proportional QALY shortfall between 0.85 and 0.95 implies a

QALY weight of 1.2. The EAG's shortfall estimates agreed with the company's and supported a severity modifier with a 1.2 QALY weighting. They confirmed that the 1.2 QALY weight also applied when considering both the second-line analyses (see [section 3.3](#)) and progression-free utility value based on COSMIC-311 (see [section 3.8](#)). So, the committee concluded that the severity weight of 1.2 applied to the QALYs was appropriate.

Cost-effectiveness estimates

Acceptable ICER

3.12 [NICE's health technology evaluations manual](#) states that, above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per QALY gained, decisions about the acceptability of the technology as an effective use of NHS resources will consider the degree of uncertainty around the ICER and any benefits of the technology that were not captured in the QALY calculations. The committee will be more cautious about recommending a technology if it is less certain about the evidence presented. The committee noted that there are no NICE-recommended second-line treatments for people with locally advanced or metastatic DTC that is unsuitable for or refractory to radioactive iodine. So, it concluded that there is an unmet need in this population (see [section 3.1](#)). But the committee also recalled that the effect of cabozantinib on OS and the resulting modelling of OS was uncertain (see [section 3.4](#) and [section 3.7](#)). The committee took this into account. It then considered that the maximum acceptable ICER would be at the lower end of the £20,000

to £30,000 per QALY gained range normally considered a cost-effective use of NHS resources.

Company and EAG cost-effectiveness estimates

3.13 The company's base-case ICER for cabozantinib plus best supportive care compared with placebo plus best supportive care was £20,166 per QALY gained when the following were applied:

- the 1.2 severity weighting
- the EAG's error correction (to include the general population utility cap; see [section 3.8](#)).

The ICER was £25,181 per QALY gained when considering the EAG's preferred analysis, which used the:

- unadjusted utility values from Fordham et al. (2015; see [section 3.8](#))
- Weibull model to extrapolate TTD for cabozantinib (see [section 3.9](#))
- adherence approach for adjusting drug acquisition costs for cabozantinib (see [section 3.10](#)).

Committee's preferred cost-effectiveness estimates

3.14 The committee agreed with the EAG's use of the Weibull model to extrapolate TTD for cabozantinib (see [section 3.9](#)). They also agreed with the adherence approach for adjusting drug acquisition costs for cabozantinib (see [section 3.10](#)) and the unadjusted post-progression utility from Fordham et al. (2015; see [section 3.8](#)). But the committee preferred to use the COSMIC-311 utility value for the progression-free health state (see [section 3.8](#)). The cost-effectiveness estimate generated by its preferred assumptions was £28,200 per QALY gained. It considered that when its preferred assumptions were incorporated, the cost-effectiveness estimate was towards the higher end of the range considered to be a cost-effective use of NHS resources. The committee would prefer to see an ICER towards the lower end of the range, because of the uncertainty in the estimate (see [section 3.12](#)). So, cabozantinib

could not be recommended for treating locally advanced or metastatic DTC that is unsuitable for or refractory to radioactive iodine, and that has progressed after systemic treatment.

Managed access

Recommendation with managed access

3.15 Having concluded that cabozantinib could not be recommended for routine use, the committee then considered if it could be recommended with managed access for previously treated locally advanced or metastatic DTC unsuitable for or refractory to radioactive iodine. The company indicated that they were not planning further data collection from COSMIC-311 and so did not submit an application for managed access. So, the committee concluded that managed access could not be considered.

Other factors

Equality issues

3.16 The committee noted the stakeholders' comments that women are more likely to be diagnosed with thyroid cancer. But the clinical experts explained that in metastatic DTC the proportions of men and women are similar. This was seen in the trial population in COSMIC-311 (see [section 3.1](#)). No other equality or social value issues were identified.

Innovation

3.17 The committee considered if cabozantinib was innovative. It did not identify additional benefits of cabozantinib not captured in the economic modelling. So, the committee concluded that all additional benefits of cabozantinib had already been taken into account.

Conclusion

Recommendation

3.18 The committee concluded that there was uncertainty in the cost-effectiveness estimates. So, it considered that the maximum acceptable ICER would be at the lower end of the £20,000 to £30,000 range normally considered a cost-effective use of NHS resources. It considered that when its preferred assumptions were incorporated, the cost-effectiveness estimates for cabozantinib plus best supportive care were towards the higher end of the range considered to be a cost-effective use of NHS resources. The committee preferred to see an ICER towards the lower end of the range, because of the uncertainty in the estimate. So, cabozantinib is not recommended for treating locally advanced or metastatic DTC that is unsuitable for or refractory to radioactive iodine, and that has progressed after systemic treatment. Had cabozantinib been recommended by the committee it would have been limited to people whose condition has progressed after 1 systemic treatment.

4 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee D](#).

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The [minutes of each evaluation committee meeting](#), which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Dr Stephen Smith

Chair, technology appraisal committee D

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser and a project manager.

Rachel Ramsden

Technical lead

Victoria Kelly

Technical adviser

Celia Mayers

Project manager

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