NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Cabozantinib and vandetanib for treating medullary thyroid cancer

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

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

The appraisal 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 race, gender, disability, religion or belief, sexual orientation, age, gender reassignment, pregnancy and maternity?

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

After consultation:

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

For further details, see NICE's guide to the processes of technology appraisal.

The key dates for this appraisal are:

Closing date for comments: 14 September 2017

Second appraisal committee meeting: 27 September 2017

Details of membership of the appraisal committee are given in section 5.

1 Recommendations

1.1 Cabozantinib is not recommended, within its marketing authorisation, for treating progressive medullary thyroid cancer in adults with unresectable, locally advanced or metastatic disease.

1.2 Vandetanib is not recommended, within its marketing authorisation, for treating aggressive and symptomatic medullary thyroid cancer in adults with unresectable, locally advanced or metastatic disease.

1.3 These recommendations are not intended to affect treatment with cabozantinib or vandetanib that was started in the NHS before this guidance was published. People having treatment outside these recommendations 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

Cabozantinib and vandetanib are the only systemic treatment options for unresectable, locally advanced or metastatic medullary thyroid cancer. Both drugs are currently available through the Cancer Drugs Fund for progressive and symptomatic disease. Best supportive care is the only other available option for people who cannot have cabozantinib or vandetanib.

Clinical trial evidence suggests that cabozantinib and vandetanib are effective in delaying disease progression but may not prolong survival. Both drugs are associated with substantial side effects, so they are only used when the disease has become symptomatic and the benefits of treatment outweigh the burden of side effects. In practice, the choice of cabozantinib or vandetanib depends mainly on their toxicity profiles rather than any perceived difference in their effectiveness.

Cost-effectiveness estimates for both cabozantinib and vandetanib are much higher than what NICE normally considers to be an acceptable use

of NHS resources (that is, between £20,000 and £30,000 per quality-adjusted life year gained). Neither treatment meets NICE's end-of-life criteria or is suitable for use in the Cancer Drugs Fund. Therefore, neither cabozantinib nor vandetanib can be recommended as a cost-effective use of NHS resources.

2 The technologies

	Cabozantinib (Cometriq, Ipsen)	**Vandetanib (Caprelsa, SanofiGenzyme)**
Marketing authorisations	Adults with progressive, unresectable locally advanced or metastatic medullary thyroid cancer. For patients in whom rearranged during transfection mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision.	Treatment of aggressive and symptomatic medullary thyroid cancer in patients with unresectable locally advanced or metastatic disease. For patients in whom rearranged during transfection mutation status is not known or is negative, a possible lower benefit should be taken into account before individual treatment decision.
Recommended doses and schedules	140 mg taken orally once daily until patient is no longer clinically benefitting from therapy or until unacceptable toxicity occurs. Dose reductions of 100 mg or 60 mg are available if needed.	300 mg taken orally once daily until disease progression or until the benefits of treatment continuation no longer outweigh its risk. Dose reductions of 200 mg or 100 mg are available if needed.
Price	£4,800 per 84x20 mg pack, 28x20 mg + 28x80 mg pack and 84x20 mg + 28x80 mg pack (excluding VAT; British national formulary July 2017). The company has agreed a patient access scheme with the Department of Health. If cabozantinib had been recommended, this scheme would provide a simple discount to the list price of cabozantinib with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme would not	£5,000 per 30x300 mg pack, or £2,500 per 30x100 mg pack (excluding VAT; British national formulary July 2017). The company has agreed a patient access scheme with the Department of Health. If vandetanib had been recommended, this scheme would provide a simple discount to the list price of vandetanib with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence. The Department of Health considered that this patient access scheme would not constitute an excessive

	constitute an excessive administrative burden on the NHS.	administrative burden on the NHS.

3 Committee discussion

The appraisal committee (section 5) considered evidence from a number of sources. See the committee papers for full details of the evidence.

The condition and current treatment

There is a clinical need for active treatments for unresectable, locally advanced or metastatic medullary thyroid cancer

3.1 Medullary thyroid cancer is rare and around 25% of cases are hereditary. The most common symptoms, such as diarrhoea and fatigue, can significantly impair patients' quality of life and wellbeing. The patient experts commented that in the absence of a cure, patients would welcome treatments that delay disease progression and control symptoms. The committee noted that cabozantinib and vandetanib are the only systemic treatment options for unresectable, locally advanced or metastatic medullary thyroid cancer, and are only available through the Cancer Drugs Fund for people with progressive and symptomatic disease. The clinical experts explained that both treatments are associated with side effects, so not all patients will be able to tolerate them. The only alternative for these people is best supportive care. The committee concluded that there is a clinical need for active treatment options for unresectable, locally advanced or metastatic medullary thyroid cancer.

Clinical trial evidence

The clinical trial evidence for cabozantinib is relevant to UK clinical practice

3.2 Evidence for the clinical effectiveness of cabozantinib was from EXAM, a double-blind, randomised controlled trial comparing cabozantinib with placebo. The trial included 330 patients with unresectable, locally

advanced, metastatic and progressive medullary thyroid cancer. The clinical experts advised that in practice, targeted treatment with cabozantinib or vandetanib is only considered for progressive and symptomatic disease, so the patients in EXAM represented those that would be seen in clinical practice. The committee concluded that the EXAM trial is relevant to UK clinical practice.

Evidence for vandetanib is less relevant to UK practice so the company presented subgroup analyses

3.3 Evidence for the clinical effectiveness of vandetanib was from ZETA, a double-blind, randomised controlled trial comparing vandetanib with placebo. The trial included 331 patients with unresectable, locally advanced and metastatic medullary thyroid cancer. The inclusion criteria were not restricted to progressive disease, so the trial included patients with less severe disease than that covered by the marketing authorisation, and patients in EXAM (and therefore patients that would not be considered for targeted treatment in clinical practice). To address this, the company presented clinical-effectiveness data for 2 subgroups from ZETA:

- the marketing authorisation subgroup, comprising patients with progressive and symptomatic disease (the 'MA subgroup')
- the restricted marketing authorisation subgroup, comprising patients from the MA subgroup who also had calcitonin (CTN) and carcinoembryonic antigen (CEA) doubling times of 24 months or less (the 'restricted MA subgroup').

The evidence for vandetanib in the MA subgroup is most relevant to UK clinical practice

3.4 The company considered the restricted MA subgroup to represent patients in most need of treatment, and therefore those seen in clinical practice. The clinical experts explained that CTN and CEA biomarkers are regularly monitored, can be prognostic and may contribute to a decision to

conduct imaging, but the decision to start treatment itself is based on radiological progression, or when the disease becomes symptomatic, or both. The assessment group considered the baseline characteristics of the MA subgroup to be comparable to the baseline characteristics of patients in EXAM, which the committee had concluded reflected patients seen in clinical practice. Having heard from the clinical experts and the assessment group, the committee concluded that the MA subgroup was most likely to represent patients seen in practice and therefore the appropriate population on which to focus its decision-making. It agreed that the restricted MA subgroup was not relevant to this appraisal and so it would not be considered further.

Subgroups

RET mutation status is not an appropriate subgroup for consideration

3.5 The marketing authorisations for both drugs specify that a possible lower benefit should be taken into account for patients in whom rearranged during transfection (RET) mutation status is negative or unknown. The committee was aware that germline RET mutation testing is standard practice to identify hereditary disease, but that somatic RET mutation testing (to identify RET mutations in those with sporadic or non-hereditary disease) is not funded in the NHS. The clinical experts explained that RET mutation testing is not done to inform treatment decisions. The committee therefore concluded that it was not appropriate to consider the clinical or cost effectiveness of either drug based on patients' RET mutation status.

Clinical trial results: EXAM (cabozantinib)

Cabozantinib improved progression-free survival compared with placebo, but the exact overall survival benefit is difficult to establish

3.6 The results showed a statistically significant benefit for cabozantinib compared with placebo for the primary outcome of centrally assessed median progression-free survival, which was 11.2 months for cabozantinib

and 4.0 months for placebo (hazard ratio [HR] 0.28; 95% confidence interval [CI] 0.19 to 0.40), with a median trial follow-up of 13.9 months. Overall survival was 26.6 months for cabozantinib and 21.1 for placebo but this was not statistically significant (HR 0.85; 95% CI 0.64 to 1.12), with a median trial follow-up of 52 months. The committee noted that patients in both arms of the trial had subsequent cancer treatments after progression which may have confounded the overall survival results, although it could not be certain to what extent. The committee concluded that cabozantinib improved progression-free survival compared with placebo, but that the exact overall survival benefit is difficult to establish.

Clinical trial results: ZETA (vandetanib)

Vandetanib improved progression-free survival compared with placebo but the exact benefit is uncertain; overall survival results are confounded and not appropriate for decision-making

3.7 ZETA was designed in such a way that patients with progressed disease (at investigator-assessed progression) in the placebo arm could switch to open-label vandetanib, and those in the vandetanib arm could continue with open-label vandetanib. In its submission the company noted that because of this, the trial results may represent the effectiveness of immediate vandetanib compared with delayed vandetanib, which the committee considered did not represent how the drug would be used in UK clinical practice. The results from the MA subgroup analysis showed a statistically significant benefit for vandetanib compared with placebo for the primary outcome of centrally reviewed median progression-free survival, which was 28.0 months for vandetanib and 16.4 months for placebo (HR 0.47; 95% CI 0.29 to 0.77), with a median trial follow-up of 24 months. The investigator-assessed median progression-free survival was 22.1 months for vandetanib and 8.3 months for placebo (HR 0.33; 95% CI 0.20 to 0.53). The committee considered that the substantial difference between the centrally reviewed and investigator-assessed results showed that although most patients whose disease progressed in

the placebo arm had crossed over to have vandetanib, it appeared that some patients may have crossed over before their disease had progressed, although the proportion is unknown. The committee therefore concluded that vandetanib improved progression-free survival compared with placebo, but that the exact benefit was difficult to establish. The overall survival benefit for vandetanib compared with placebo was not statistically significant, with a median follow-up of 105 months (results are academic in confidence and cannot be reported here). Neither the company nor the assessment group were able to adjust the trial results for treatment switching, meaning that the overall survival results presented were confounded and not reliable. The committee concluded that because the overall survival results were confounded and difficult to interpret, they were not appropriate to inform its decision-making.

Indirect treatment comparison

Cabozantinib and vandetanib are likely to be similarly effective

3.8 The assessment group's network meta-analysis comparing cabozantinib with vandetanib showed that in terms of progression-free survival the 2 treatments were broadly similar. However, because of the sparsity of the network, the assessment group did not consider the results robust enough to use in the economic model. The assessment group did not include overall survival in the analysis because of the significant crossover in ZETA. The clinical experts stated that in their opinion, both drugs have similar effectiveness in terms of delaying progression and controlling symptoms, although there is no evidence to show that they prolong survival. They explained that the decision about whether to use cabozantinib or vandetanib in clinical practice related more to their differing toxicity profiles than their relative effectiveness. The committee concluded that in the absence of more robust comparative data, cabozantinib and vandetanib were likely to be similarly effective.

There is insufficient evidence for the effectiveness of sequential treatment with cabozantinib and vandetanib

3.9 The committee understood that second-line treatment with a tyrosine kinase inhibitor (TKI, such as cabozantinib and vandetanib) was not available in the Cancer Drugs Fund, because the criteria allow for switching to another TKI only when there is intolerance to the first and the disease has not progressed. It noted that about 20% of patients in EXAM had had a previous TKI (about half of whom had vandetanib), and that a subgroup analysis suggested consistent progression-free survival benefit regardless of previous TKI therapy. However, the committee concluded that there was insufficient data to show that cabozantinib and vandetanib are effective when used sequentially (that is, after another TKI) after disease progression.

Adverse events

Adverse events are common with both drugs and the decision to use them is based on careful consideration of the risks and benefits

3.10 All patients in EXAM and almost all (99.6%) of the patients in ZETA had an adverse event while having cabozantinib or vandetanib. The committee was aware that patients with unresectable, locally advanced or metastatic medullary thyroid cancer have a substantial disease burden, demonstrated by high levels of adverse events in the placebo arms of both trials and the comorbidities of patients shown in the baseline characteristics data. The patient expert described side effects such as frequent diarrhoea, rash and fatigue, but considered that the disease would have had a more severe effect without treatment. The clinical experts explained that treatment toxicities tend to occur soon after treatment starts, and that for most patients the dosage is reduced after the initial treatment period. The experts explained the importance of balancing the risks and benefits when considering starting treatment with either cabozantinib or vandetanib, and that treatment is usually started only

when the disease becomes symptomatic to the extent that the benefits of treatment outweigh the burden of side effects.

Economic models

The company's economic model for vandetanib is not appropriate for decision-making

3.11 The company's economic analysis for vandetanib was based only on the restricted MA subgroup from ZETA. Having previously concluded that the restricted MA subgroup did not reflect UK clinical practice and would not be considered further (section 3.4), the committee concluded that the company's economic model for vandetanib was not appropriate for decision-making.

The assessment group's economic model comprised 5 analyses, 4 of which were appropriate for consideration

3.12 The assessment group presented 5 analyses for the cost effectiveness of cabozantinib and vandetanib compared with best supportive care and with each other, using a partitioned survival model:

- Analysis 1: pairwise comparison of cabozantinib and best supportive care.
- Analysis 2: pairwise comparison of vandetanib (MA subgroup) and best supportive care.
- Analysis 3: incremental comparison of all treatment options using EXAM trial data, applying the vandetanib (MA subgroup) progression-free survival treatment effect to the placebo arm of EXAM and assuming the same overall survival benefit for both vandetanib and cabozantinib.
- Analysis 4: incremental comparison of all treatment options using EXAM trial data, assuming the same progression-free and overall survival benefit for both vandetanib and cabozantinib.

- Analysis 5: pairwise comparison of vandetanib (restricted MA subgroup) and best supportive care.

The committee did not consider analysis 5 to be relevant because it used the restricted MA subgroup. The committee concluded that the rest of the analyses in the assessment group's economic model were appropriate for consideration because they included the patient population that reflected UK clinical practice.

Costs

Analyses including vandetanib effectiveness data from ZETA and costs after progression do not reflect clinical practice so are not appropriate

3.13 To reflect the open-label use of vandetanib in ZETA, the assessment group included the costs of treatment with vandetanib after disease progression in both arms of analysis 2. The committee understood that including the costs of treatment after progression was necessary because from the data available the assessment group could not adjust for treatment switching. The assessment group explained that because this analysis used a partitioned survival model, after disease progression patients could only transition to the death state. This had the effect of treatment after disease progression continuing until death. The committee agreed that this resulted in an unrealistic overestimation of costs after disease progression, which was greater in the placebo arm than in the vandetanib arm of analysis 2. The clinical experts stated that if imaging shows disease progression, clinicians would normally stop treatment. They explained that treatment may continue if imaging showed only 1 lesion growing and others to be stable, but emphasised that this was uncommon and treatment would only continue for another 1 or 2 months. The committee considered that when treatment with vandetanib has stopped working, quality of life would actually be improved by stopping treatment because of its associated toxicities. It therefore concluded that treatment after disease progression does not reflect clinical practice,

meaning that analyses including vandetanib effectiveness data from ZETA and treatment costs after disease progression were not appropriate for decision-making.

The assessment group's application of the vandetanib discontinuation parameter is acceptable

3.14 The assessment group considered the company's method of applying the vandetanib pre-progression discontinuation parameter in the model to be inappropriate, because it removed all the costs of vandetanib from the proportion of patients who discontinued treatment in the pre-progression state. The assessment group acknowledged that treatment discontinuation may happen early, but stated it was unrealistic that no vandetanib costs would be incurred for patients who discontinued treatment and that this led to pre-progression vandetanib costs being underestimated. The assessment group instead applied half the costs of vandetanib to the proportion of patients who discontinued treatment pre-progression; in the absence of data showing when patients discontinued treatment, the committee considered this was an acceptable approach.

Monitoring costs used by the assessment group were more appropriate than those used by the company

3.15 In all analyses the assessment group assumed fewer outpatient appointments than the company had in its model (6.0 per year compared with 36.5 per year). The clinical experts considered 36.5 to be an overestimate of what is seen in clinical practice. They confirmed that patients were seen about once a month, although this varies because open access clinics are also available. Having heard all relevant clinical expert advice, the committee concluded that the monitoring costs estimated by the assessment group were more reasonable than those estimated by the company.

Utility values

Utility values for medullary thyroid cancer are unknown but the approach used by the assessment group is acceptable

3.16 There are no direct estimates of health utilities for people with medullary thyroid cancer. For pre-progression utility values, the company mapped data from the ZETA trial to the EQ-5D; for post-progression utility values it used data from Beusterien et al. (2009), a study of melanoma. The assessment group stated its preference to use the same source of data for both pre- and post-progression utility values, and so used values from Fordham et al. (2015), a study of differentiated thyroid cancer, for both. The committee noted that differentiated thyroid cancer was different to medullary thyroid cancer, but acknowledged that the only other potentially relevant study available was in melanoma, which is more uncertain. It noted that Fordham et al. had been used in a previous health technology assessment submission relating to thyroid cancer, and heard from the assessment group that because of low post-progression utility values it was the most favourable source of utility data for both cabozantinib and vandetanib. The committee agreed that it was difficult to determine a preferable source of health utility data and in the absence of any data relevant to medullary thyroid cancer it would accept the assessment group's estimates.

Cost-effectiveness estimates for cabozantinib

Analyses 1 and 4 are the most appropriate scenarios to assess the cost effectiveness of cabozantinib

3.17 The assessment group took the clinical parameters for analyses 1 and 4 from the EXAM trial, which the committee considered to be reflective of UK clinical practice in terms of patient population (section 3.2) and stopping treatment at disease progression (section 3.13). The committee therefore concluded that these were the most robust cost-effectiveness analyses for cabozantinib.

The most plausible ICER for cabozantinib is higher than the range normally considered cost effective

3.18 Including the confidential patient access scheme discount, the probabilistic incremental cost-effectiveness ratio (ICER) for cabozantinib compared with best supportive care was significantly higher than £30,000 per quality-adjusted life year (QALY) gained in both analyses 1 and 4 (the exact ICERs are commercial in confidence and cannot be reported here). The committee was aware that the survival functions used by the assessment group in these analyses represented the second most favourable extrapolation of long-term survival for people having cabozantinib, and that these analyses may be optimistic estimates of cost effectiveness. The committee concluded that the most plausible ICER was higher than what NICE normally considers to be a cost-effective use of NHS resources (that is, between £20,000 and £30,000 per QALY gained).

Cost-effectiveness estimates for vandetanib

Analysis 4 is the most plausible scenario to assess the cost effectiveness of vandetanib but there remains some uncertainty

3.19 Having previously concluded that neither the restricted MA subgroup (section 3.12) nor any analyses using vandetanib effectiveness data from ZETA or costs after progression (section 3.13) were relevant, the committee agreed that analyses 2, 3 and 5 were not appropriate for its decision-making. The committee noted that analysis 4 relied on strong assumptions about the equivalence of cabozantinib and vandetanib in terms of efficacy. However, having heard clinical advice that the choice of which drug to use is based more on toxicity profiles than effectiveness, and that clinicians generally do not prefer one over the other, the committee had itself concluded that cabozantinib and vandetanib were likely to be similarly effective (section 3.8). It was aware that both drugs were available through the Cancer Drugs Fund based on the same trial evidence reviewed by the appraisal committee, and acknowledged the importance for patients with specific characteristics to have a choice of

treatment. Therefore, in the absence of any other appropriate analysis for vandetanib, the committee concluded that analysis 4, which assumed the same progression-free and overall survival benefit for cabozantinib and vandetanib, represented the most plausible scenario to assess the cost effectiveness of vandetanib, although this is subject to some uncertainty.

The most plausible ICER for vandetanib is higher than the range normally considered cost effective

3.20 Including the confidential patient access scheme discount, the probabilistic ICER from analysis 4 for vandetanib compared with cabozantinib was significantly higher than £100,000 per QALY gained (the exact ICERs are commercial in confidence and cannot be reported here). The committee was aware that the survival functions used by the assessment group in this analysis represented the second most favourable extrapolation of long-term survival for people having vandetanib, and that this analysis may be an optimistic estimate of cost effectiveness. The committee concluded that the most plausible ICER was much higher than what NICE normally considers to be a cost-effective use of NHS resources (that is, between £20,000 and £30,000 per QALY gained).

Uncaptured benefits

There are no health-related benefits that are not captured in the analyses

3.21 The committee acknowledged the company's comments that vandetanib was the first systemic therapy for medullary thyroid cancer to gain a marketing authorisation, but it did not consider that the available evidence had demonstrated any substantial clinical benefit. The committee recognised that medullary thyroid cancer is rare, and that cabozantinib and vandetanib are the only targeted treatments available in this indication. However, it heard from the clinical experts that the survival benefit of both drugs is unknown, and so treatment aims to delay disease progression and improve quality of life. The committee acknowledged that

although both drugs may work well for some people, for many others there will be a substantial side-effect burden. The committee acknowledged the small patient population covered by the marketing authorisations for cabozantinib and vandetanib. It noted the advice from NICE's social value judgements: principles for the development of NICE guidance, that NICE should evaluate drugs to treat rare conditions in the same way as any other treatment. It therefore concluded that there are no additional health-related quality-of-life benefits not already captured in the QALY calculations.

End of life

Both drugs meet the end-of-life criterion for extension to life

3.22 The committee considered the advice about life-extending treatments for people with a short life expectancy in NICE's Cancer Drugs Fund technology appraisal process and methods. The EXAM trial showed overall survival benefit of more than 3 months for cabozantinib compared with placebo. The ZETA trial results in the relevant patient population were confounded and not generalisable (sections 3.7 and 3.13). The model estimated a mean survival benefit of about 7 months, and so the committee agreed that the end-of-life criterion for extension to life was met for cabozantinib. Given the expected similarity in the drugs' efficacy (see section 3.8), the committee concluded that vandetanib could also be considered to meet this criterion.

Neither drug meets the short life expectancy criterion for end of life so the end-of-life criteria do not apply

3.23 For the short life expectancy criterion, the assessment group's model predicted a mean overall survival with best supportive care of over 24 months (about 47 months in the base-case analyses), regardless of the parametric function used to extrapolate survival. However, the committee was aware in EXAM, median overall survival in the placebo arm was less than 24 months. It acknowledged that some patients with unresectable,

locally advanced or metastatic medullary thyroid cancer live for a long time. This may have skewed the median estimate, and may explain the difference between the median and mean estimates. The committee agreed that the mean estimate was more relevant for end-of-life considerations. Taking this into account, the committee concluded that neither cabozantinib nor vandetanib met the criterion for short life expectancy, and therefore the end-of-life criteria did not apply.

Recommendations

3.24 The committee could not recommend cabozantinib and vandetanib as a cost-effective use of NHS resources for treating medullary thyroid cancer, because the ICERs for both drugs were significantly higher than £30,000 per QALY gained, and neither drug met the end-of-life criteria.

Cancer Drugs Fund

Sanofi proposed that vandetanib could be used in the Cancer Drugs Fund for data collection

3.25 Having concluded that neither cabozantinib nor vandetanib could be recommended for routine use, the committee then considered if it could recommend the treatments for use in the Cancer Drugs Fund. The committee discussed the new arrangements for the Cancer Drugs Fund agreed by NICE and NHS England in 2016, noting the addendum to the NICE process and methods guides.

- Ipsen did not consider cabozantinib to have potential use in the Cancer Drugs Fund, because not enough patients would have the drug to enable data collection to address the uncertainties in the clinical-effectiveness evidence.
- Sanofi expressed an interest in vandetanib being considered for use in the Cancer Drugs Fund. It proposed that data on the baseline characteristics of patients could be collected to address uncertainty about the nature of the patient population having vandetanib in clinical

practice in England: specifically whether it was patients with progressive and symptomatic disease (the MA subgroup), or patients with progressive and symptomatic disease and CTN/CEA doubling times of 24 months or less (the restricted MA subgroup).

Neither drug fits the criteria for inclusion in the Cancer Drugs Fund

3.26 The committee had previously concluded that CTN/CEA doubling times were not used to initiate treatment with vandetanib (section 3.4), which the company had also acknowledged in its response to consultation on the assessment group report. The committee therefore did not consider there was a benefit to the NHS from collecting data on patient characteristics. The key uncertainties in the clinical-effectiveness evidence for vandetanib related to overall survival benefit, and the committee considered that not enough patients would have vandetanib to allow for data collection to address this uncertainty. The committee also did not consider that there was plausible potential to satisfy the criteria for routine use because the most plausible ICERs were substantially above the level at which NICE normally considers to be a cost-effective use of NHS resources. Therefore it concluded that neither vandetanib nor cabozantinib met the criteria for inclusion in the Cancer Drugs Fund.

Equalities

3.27 No equality issues were identified.

4 Proposed date for review of guidance

4.1 NICE proposes that the guidance on this technology is considered for review by the guidance executive 3 years after publication of the guidance. NICE welcomes comment on this proposed date. The guidance executive will decide whether the technology should be reviewed based on information gathered by NICE, and in consultation with consultees and commentators.

Professor Gary McVeigh
Chair, appraisal committee D
August 2017

5 Appraisal committee members and NICE project team

Appraisal 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 to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

The minutes of each appraisal committee meeting, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

The technology appraisal committees are standing advisory committees of NICE. This topic was considered by members of the existing standing committees who have met to reconsider drugs funded by the Cancer Drugs Fund. The names of the members who attended are in the minutes of the appraisal committee meeting, which are posted on the NICE website.

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

NICE project team

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

Anna Brett

Technical lead

Nwamaka Umeweni

Technical adviser

Kate Moore

Project manager

ISBN: [to be added at publication]