NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Appraisal consultation document

Brigatinib for treating ALK-positive advanced non-small-cell lung cancer after crizotinib

The Department of Health and Social Care has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using brigatinib in the NHS in England. The appraisal committee has considered the evidence submitted by the company 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?

Issue date: September 2018

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 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 document.
- Subject to any appeal by consultees, the final appraisal document may be used as the basis for NICE's guidance on using brigatinib 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: 24 October 2018

Second appraisal committee meeting: 8 November 2018

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

1 Recommendations

1.1 Brigatinib is not recommended, within its anticipated marketing authorisation, for treating anaplastic lymphoma kinase (ALK)-positive advanced non-small-cell lung cancer (NSCLC) in adults who have already had crizotinib.

1.2 This recommendation is not intended to affect treatment with brigatinib 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

People with ALK-positive advanced NSCLC that has been treated with crizotinib are currently offered ceritinib as their next treatment.

Clinical evidence based on single-arm studies suggests that people having brigatinib live longer than those having ceritinib, and that they live longer before their condition worsens.

The company's results from its cost-effectiveness modelling are optimistic and the company's assumption about the length of treatment benefit of brigatinib is clinically implausible. Also, the most plausible cost-effectiveness estimates for brigatinib compared with ceritinib are above what NICE normally considers acceptable for an end-of-life treatment.

Therefore, brigatinib cannot be recommended to treat ALK-positive advanced NSCLC.

2 Information about brigatinib

Anticipated marketing authorisation indication	On 20 September 2018 brigatinib (Alunbrig, Takeda Pharmaceuticals) received a positive opinion from the Committee for Human Medicinal Products, recommending the granting of a marketing authorisation, intended for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer previously treated with crizotinib.
Dosage in the marketing authorisation	The proposed recommended starting dosage of brigatinib is 90 mg once daily for the first 7 days, then 180 mg once daily. Treatment should continue as long as there is clinical benefit. If brigatinib treatment is interrupted for 14 days or longer for reasons other than adverse reactions, treatment should be resumed at 90 mg once daily for 7 days before increasing to the previously tolerated dose. If a dose is missed or vomiting occurs after taking a dose, an additional dose should not be administered, and the next dose should be taken at the scheduled time.
Price	The proposed list price for brigatinib is: £4,900 for the recommended dose (180mg/day) for 1 pack of 28 tablets of 180 mg per day or a starter pack (7 x 90 mg + 21 x 180 mg). The company has a commercial arrangement, which would have applied if the technology had been recommended.

3 Committee discussion

The appraisal committee (section 5) considered evidence submitted by Takeda Pharmaceuticals and a review of this submission by the evidence review group (ERG). See the committee papers for full details of the evidence.

Clinical need

A new treatment option would benefit people with ALK-positive advanced NSCLC

3.1 People with anaplastic lymphoma kinase (ALK)-positive advanced non-small-cell lung cancer (NSCLC) tend to be younger and are less likely to

have a history of smoking than the wider NSCLC population. The patient experts explained that ALK-positive advanced NSCLC is debilitating, and that people with the condition worry about poor outcomes. They also highlighted that an improved quality of life, better management of symptoms and an increase in how long they live is very important to people with the condition and their families. The clinical experts acknowledged that an additional treatment option would be beneficial if it offered better tolerability than existing treatments. The committee understood that additional options are beneficial for ALK-positive advanced NSCLC, and concluded that brigatinib could be a useful option if it is better tolerated than existing treatments.

Treatment pathway and relevant comparators

Ceritinib is the relevant comparator for this appraisal

3.2 NHS England explained that ALK-status testing is now routine clinical practice, so status is known before starting treatment. Therefore, the committee agreed to focus its discussion on the pathway in which ALK-status is known before starting treatment. The committee understood that crizotinib, ceritinib and alectinib are options for people with untreated ALK-positive advanced NSCLC. The clinical experts explained that fewer people are starting treatment on crizotinib because of the availability of ceritinib and alectinib. Therefore, the population eligible for brigatinib after crizotinib is small and will decrease as fewer people start treatment with crizotinib. The committee was aware that NICE has recommended ceritinib as a subsequent treatment option when NSCLC progresses with crizotinib. It therefore concluded that ceritinib was the only relevant comparator for brigatinib in people with ALK-positive advanced NSCLC who have had treatment with crizotinib.

Clinical evidence

The main evidence for brigatinib is from 2 single-arm studies and is broadly generalisable to UK clinical practice

3.3 There were no studies or clinical trials that directly compare brigatinib with ceritinib. The main clinical evidence for brigatinib came from 2 single-arm studies:

- ALTA, a phase II study including 110 people in the study arm using the dose in line with the marketing authorisation for this appraisal.
- Study-101, a phase I/II study including 25 people in the relevant subgroup.

The primary outcome in both studies was investigator-assessed overall response rate, using Response Evaluation Criteria in Solid Tumors (RECIST v1.1). Secondary outcomes in the studies included progression-free and overall survival, safety and tolerability and duration of response. The median follow-up in ALTA was 24.3 months and median overall survival was 34.1 months. Objective response rate was 56% in ALTA and 76% in Study-101 (investigator-assessed). Median progression-free survival was 16 months in ALTA and Study-101 (investigator-assessed). Median duration of response was 14 months (investigator-assessed) and 16 months (independent review committee-assessed) in ALTA and 26 months in Study-101 (investigator-assessed). The committee heard that 74% of people in ALTA had previously had chemotherapy and 67% had brain metastases before starting the study. The clinical experts confirmed that the ALTA population broadly reflected people with ALK-positive advanced NSCLC in England. The committee acknowledged that, because there was no head-to-head evidence with the relevant comparator ceritinib, an indirect treatment comparison would be the only way to judge the relative effectiveness of brigatinib compared with ceritinib (see section 3.6). The committee concluded that, although most people in

the studies had had previous chemotherapy, ALTA and Study-101 provided evidence that was generalisable enough to clinical practice for decision-making.

The main evidence for the comparator, ceritinib, comes from ASCEND-2 and ASCEND-5

3.4 The main clinical evidence for ceritinib came from 2 studies:

- ASCEND-2, a single-arm phase II study including 140 people.
- ASCEND-5, a randomised controlled phase III trial including 231 people in the ceritinib arm.

Only 1 arm of the ASCEND-5 study was used in the analysis. This was because its comparator (chemotherapy) was not in the appraisal scope because ALK-status testing is now routine practice in England. The primary outcome in ASCEND-5 was independent review committee-assessed progression-free survival, using RECIST v1.1, and overall survival was included as a secondary outcome. The primary outcome in ASCEND-2 was investigator-assessed objective response rate, using RECIST v1.1. Secondary outcomes in ASCEND-2 included overall and progression-free survival. The committee accepted that ASCEND-2 and ASCEND-5 were appropriate studies to be considered for the comparator in this appraisal.

Treatment with an ALK inhibitor may continue after disease progression

3.5 In ALTA treatment could continue after disease progression if there was clinical benefit, as determined by the trial investigator. The clinical experts said that this reflects clinical practice in England for both brigatinib and ceritinib. They explained that treatment is continued after disease progression because the treatment might control cancer at sites other than the lungs. The company stated that it did not have any data from ALTA that gave the reasons for stopping treatment. The committee

concluded that, in current practice, treatment with brigatinib and ceritinib continues after disease progression.

Indirect comparison of brigatinib and ceritinib

An indirect comparison is appropriate because there are no head-to-head trials comparing brigatinib with ceritinib

3.6 Because there were no head-to-head trials comparing brigatinib with ceritinib, the company did an unanchored indirect treatment comparison (ITC). Results from the 4 single-arm studies (see section 3.3 and section 3.4) were used, and 2 approaches were taken: a naive ITC and a matching-adjusted indirect comparison (MAIC). The MAIC adjusts for differences in baseline characteristics between study populations whereas naive ITC analyses do not. The company presented several analyses using both the naive ITC and MAIC approaches. For overall survival these were:

- Using combined data for brigatinib (including ALTA and Study-101) and using separate data for ceritinib (that is, analyses using either ASCEND-2 or ASCEND-5).
- Using only ALTA data for brigatinib, and using separate data for ceritinib (that is, analyses using either ASCEND-2 or ASCEND-5).

Progression-free survival was not reported as an investigator-assessed outcome in ASCEND-5 or as an independent review committee-assessed outcome in Study-101. Therefore, the company presented the results using:

- Combined data for brigatinib (including ALTA and Study-101) and using ASCEND-2 data for ceritinib (investigator-assessed progression-free survival).

- Only ALTA data for brigatinib and using separate data for ceritinib (that is, analyses using either ASCEND-2 or ASCEND-5) (independent review committee-assessed progression-free survival).

The ERG found the ITC analyses to be broadly appropriate given the available trial data. The ERG agreed with the company that there was broad consistency of the results between the MAIC and naive ITC approaches. The committee concluded that, given the available trial data, the company's approach was appropriate.

Meta-analysis of the indirect treatment comparison results

The meta-analyses gave consistent results that are acceptable for decision-making

3.7 For overall survival, the company did 2 meta-analyses to provide estimates of clinical effectiveness:

- It compared pooled ALTA and Study-101 data (on brigatinib) with ASCEND-2 and ASCEND-5 data (on ceritinib) separately.
- It compared data from ALTA only with ASCEND-2 and ASCEND-5 separately.

The company's preferred approach was to compare pooled ALTA and Study-101 data with ASCEND-2 and ASCEND-5 data separately. For progression-free survival, the analysis only included data from ALTA and meta-analysed the results of the ITC against the data from ASCEND-2 with ASCEND-5 separately. This was because data for independent review committee-assessed progression-free survival were not available for Study-101, and data for investigator-assessed progression-free survival was not available from ASCEND-5. The ERG was concerned that no adjustment was made to account for the brigatinib data being included twice in the meta-analysis. But overall, it was satisfied that consistent results were produced using each analytical strategy to meta-analyse the

ITC results. All approaches taken for the meta-analysis showed that brigatinib extended overall and progression-free survival compared with ceritinib, and that the difference between treatments was statistically significant. The committee noted that the results suggested brigatinib improved overall survival by 19 months and progression-free survival by 9 months compared with ceritinib. The committee acknowledged that there is uncertainty with single-arm studies and the results should be interpreted with caution. The committee concluded that the meta-analyses gave consistent results and were acceptable for decision-making.

Clinical evidence in the economic model

The results from the meta-analysis are broadly appropriate to include in the model but the progression-free survival estimate could be more robust

3.8 The company used the results of the MAIC ITC that included ALTA and Study-101 data for brigatinib and ASCEND-2 for ceritinib to estimate the progression-free survival hazard ratio between brigatinib and ceritinib (see section 3.6). The hazard ratio was then applied to the brigatinib data to estimate progression-free survival for ceritinib. The committee noted that ASCEND-5 was a larger trial (110 people compared with 25 in Study-101) and had reported independent review committee-assessed progression-free survival (see section 3.4). The ERG highlighted that ASCEND-5 was a higher quality trial and a more robust data source. The ERG preferred using the results of the meta-analysis of the MAIC ITC that included only ALTA for brigatinib compared separately with ASCEND-5 (ceritinib) and ASCEND-2 (ceritinib) (see section 3.7). The committee agreed that data from ASCEND-5 data should be included. It concluded that the ERG's approach to estimate progression-free survival was the most appropriate.

Extrapolating clinical trial data in the economic model

The company's extrapolation of brigatinib overall survival is appropriate

3.9 The company extrapolated overall survival of brigatinib in its model using the Gompertz function. This estimated that 30% of people with ALK-positive advanced NSCLC would be alive at 5 years and 6% at 10 years. The company explained that this broadly reflected estimates from its clinical advisers. The committee noted the wide range of estimates from the company's advisers. At the appraisal committee meeting, the clinical experts said that it was difficult to estimate the proportion of people with ALK-positive advanced NSCLC who would be alive at specific time points in the future, and that it was not possible to give an accurate prediction. They explained that overall survival has improved over recent years because of the use of ALK-targeted therapies. The ERG noted that the extrapolation of overall survival was very uncertain because the studies had short follow-ups, making the extrapolation periods relatively long. It highlighted that the conclusions should be treated with caution. The ERG also used the Gompertz function in its base case although it noted that a range of functions were plausible based on statistical fit. The committee heard that all other functions predicted higher survival rates than Gompertz. It concluded that, although there was some uncertainty about the long-term prognosis for this population, the company's approach of using the Gompertz function was acceptable for modelling overall survival.

The gamma and Gompertz functions are acceptable for extrapolating progression-free survival

3.10 The company extrapolated progression-free survival in its model using the Gompertz function. The ERG reported that this choice was not adequately justified by the company. Its preferred choice was the gamma function based on it being considered a better statistical fit. The committee considered a range of functions to be suitable because all of them fitted the observed period of data well (based on statistical fit). The committee

agreed that the gamma and Gompertz functions could be considered acceptable to extrapolate progression-free survival.

Time on treatment after disease progression

The company's approach to modelling time on treatment after disease progression is appropriate

3.11 The company assumed that treatment is continued for 1.53 months after disease progression for both brigatinib and ceritinib. This was estimated by calculating the difference in median time on treatment (17.15 months) and median progression-free survival (15.62 months) from ALTA. The ERG suggested that it was more appropriate to use data from ASCEND-2 to estimate treatment duration after progression for ceritinib. Therefore, the ERG included a treatment duration after progression of 1.53 months for brigatinib (based on ALTA) and of 3.10 months for ceritinib (based on ASCEND-2) in their base case. The clinical experts highlighted that treatment duration after progression would be similar for both brigatinib and ceritinib. They estimated that progressed disease would be treated for a further 2 to 3 months. The committee concluded that treatment duration after progression would be similar for brigatinib and ceritinib and that, without any better data, the company's estimate of 1.53 months was appropriate for decision-making.

Duration of treatment benefit after progression

The company assumes a lifetime of continued treatment benefit, even after treatment has stopped, but there is limited evidence to support this

3.12 The company assumed a continued treatment benefit associated with overall and progression-free survival for brigatinib and ceritinib over the full time horizon of the model. The clinical experts explained that it was reasonable to assume that treatment benefit would continue for a few months after stopping treatment. However, they said that there was limited evidence of long-term continued benefit after stopping treatment

and no known biological reason for a prolonged effect. The clinical experts explained that there may be a longer continued treatment benefit with brigatinib than ceritinib because brigatinib seems more effective in the central nervous system and offers a greater depth of response (more tumour shrinkage with brigatinib) than ceritinib. However, they highlighted that there was no evidence to directly support this and it may have been captured already in the estimate of progression-free survival. The ERG estimated continued treatment benefit by comparing each of the strategies with best supportive care. It used the point at which the rate of decline of treatment benefit was higher for brigatinib than best supportive care as the time point for when treatment effect was lost. The ERG estimated that this was 1.46 years for brigatinib and 1.07 years for ceritinib from the start of treatment. Although it attempted to take into account a shortened continued treatment benefit after progression, the analysis did not give clinically plausible outputs of survival after 3 years because the estimates were too low. Therefore the committee could not accept this approach. The committee agreed that a method similar to the ERG's modelling approach might be suitable for decision-making if the outputs of survival were clinically plausible. The committee concluded that the modelling of a lifetime continued treatment benefit was not clinically plausible in people with symptomatic ALK-positive advanced NSCLC who had stopped treatment.

Health-related quality of life

The utility value for pre-progressed disease is acceptable

3.13 The company derived the utility value for pre-progressed disease of 0.793 from ALTA. The clinical experts confirmed that this utility value was reasonable. They explained that people with ALK-positive advanced NSCLC are well, even at the end of treatment. The committee concluded that the utility value of 0.793 for pre-progressed disease was appropriate.

A decline in utility is needed for people with progressed disease after treatment is stopped

3.14 The company estimated the quality of life associated with progressed disease using published utility values. It used a utility decrement of 0.150 from Chouaid et al. (2013), giving a utility estimate of 0.643 for progressed disease. People in Chouaid et al. had general NSCLC, not specifically ALK-positive advanced disease. The committee understood that the wider NSCLC population tend to be older and have a history of smoking and are likely have a lower incidence of brain metastases than people with ALK-positive disease. The ERG noted in their submission that the mean estimate of 0.643 for progressed disease was higher than the estimates provided in the 2 included studies (Chouaid et al. 0.460; Nafees et al. 2008, 0.473). It also noted that these utility values were for the wider NSCLC population. The clinical experts explained that, even with central nervous system involvement, people with progressed ALK-positive advanced NSCLC can have a good quality of life. The committee noted that the utility value of 0.643 was applied for the full duration of progressed disease until death. The clinical experts stated that a utility value of 0.643 was reasonable when people have progressed on treatment. However, they thought it was unlikely that this value would remain constant throughout progression. They said that a decline in utility would be expected for people whose condition had progressed and treatment had stopped. The committee concluded that the company's utility value for progressed disease on treatment was reasonable, but considered that a decline in utility was needed for people with progressed disease after treatment had stopped.

Resource use and costs

Drug wastage for brigatinib and ceritinib should be included

3.15 The company assumed that there was no drug wastage (that is, the NHS would save all costs associated with the reduced dose intensity seen in

the studies). The ERG's preferred assumption was to use half the difference between the observed and expected dose for each treatment. A written statement from NHS England highlighted that there was likely to be more drug wastage with ceritinib than brigatinib. The clinical experts explained that dose reduction is common with ceritinib because of toxicity but dose reduction with brigatinib is uncommon. The committee agreed that the ERG's approach accounted for the difference in tolerability between brigatinib and ceritinib. It concluded that drug wastage for brigatinib and ceritinib should be included and that using a similar approach to the ERG's was reasonable.

It is reasonable to include drug administration and delivery costs

3.16 The company included an administration cost but no delivery cost for brigatinib and ceritinib in their model. The ERG included a delivery cost of £42.50 per item per cycle for both brigatinib and ceritinib, based on advice from a senior NHS pharmacist. The Cancer Drugs Fund (CDF) clinical lead explained that most trusts use a third-party dispenser for oral chemotherapy treatments, which incurs a cost for home delivery, and suggested that a delivery cost would be applied about 70% of the time. The CDF clinical lead also explained that, because brigatinib is a high-cost chemotherapy, the oral chemotherapy administration tariff (£120) should have been used in the company's model and included as a cost per item per cycle. The committee concluded that the administration cost of £120 given by NHS England should have been included in the modelling, and that a delivery cost should have been included for 70% of treatments to reflect variable practice across different trusts.

Cost-effectiveness results

The company's base-case ICER comparing brigatinib with ceritinib is greater than £50,000 per QALY gained

3.17 The committee considered the incremental cost-effectiveness ratios (ICERs) from the company's base case, recalculated by the ERG to include the approved patient access scheme discounts for brigatinib and ceritinib (which are confidential so the ICERs cannot be reported here). The company's base-case ICER for brigatinib compared with ceritinib was above £50,000 per quality-adjusted life year (QALY) gained. The committee concluded that the company's base case was not appropriate for decision-making because of concerns about the following inputs and assumptions in the model:

- the continued treatment benefit assumption (see section 3.12)
- the data and extrapolation used to estimate progression-free survival (see section 3.8 and section 3.10)
- the utility estimate for progressed disease after treatment had stopped (see section 3.14)
- the wastage assumption (see section 3.15)
- the administration and delivery cost assumptions (see section 3.16).

The ERG's preferred assumptions increase the ICER

3.18 The ERG's preferred assumptions included using:

- treatment after progression based on estimates from clinical trials (brigatinib, 1.53 months; ceritinib, 3.20 months)
- treatment benefit up to the predicted decline in effect compared with standard of care (brigatinib, 1.46 years; ceritinib, 1.07 years)
- the hazard ratio from the meta-analysis for progression-free survival that included independent review committee-assessed estimates from each of the studies

- a gamma distribution to extrapolate progression-free survival
- drug wastage assuming that only half of the wastage is financially recoverable
- a drug delivery cost of £42.50 per item.

The committee noted that combining the ERG's preferred assumptions substantially increased the ICERs compared with the company's base case. The ERG's base-case with its preferred assumptions gave an ICER for brigatinib compared with crizotinib that was substantially more than £50,000 per QALY gained.

The most plausible ICER is higher than £50,000 per QALY gained

3.19 Having considered the ICERs using the ERG's preferred assumptions, the committee took into account its preferred assumptions that differed from the ERG's base case. These included using:

- the same time on treatment after progression for both treatments, as estimated by the company (1.53 months; see section 3.11)
- progression-free survival extrapolated using Gompertz (see section 3.10)
- a decline in the utility value for progressed disease after treatment had stopped (see section 3.14)
- administration costs of £120 per item per cycle and a delivery cost for 70% of treatments (see section 3.16).

The committee recalled that the ERG's approach of modelling shorter continued treatment benefit after progression did not provide clinically plausible estimates of survival after 3 years (see section 3.12). The committee understood that shortening the treatment benefit would increase the ICER substantially. It concluded that the most plausible ICER for brigatinib compared with ceritinib in people with ALK-positive advanced NSCLC was above £50,000 per QALY gained.

End of life

Life expectancy for people with ALK-positive advanced NSCLC is considered to be around 24 months

3.20 The committee considered advice about life-extending treatments for people with a short life expectancy in NICE's guide to the methods of technology appraisal. The company considered that the life expectancy of people with ALK-positive advanced NSCLC would be less than 24 months, thereby meeting the first criterion for an end-of-life treatment. Median life expectancy reported in ASCEND-2 was 14.9 months and in ASCEND-5 it was 18.1 months. Mean overall survival was not reported in ASCEND-2 and ASCEND-5. The company's model predicted a mean overall survival for people with ALK-positive advanced NSCLC of around 24 months. The committee concluded that the life expectancy of people with ALK-positive advanced NSCLC having ceritinib is around 24 months.

Brigatinib extends life by at least 3 months

3.21 The company estimated a mean life extension of 22.49 months with brigatinib, which meets the second criterion for an end-of-life treatment. The company's estimate depended on a lifetime continued treatment benefit that was considered an optimistic approach by the committee (see section 3.12). Also, the committee understood that estimating overall survival for this population is very uncertain (see section 3.9). The ERG highlighted that the data used to estimate the extension to life were not robust but that extension to life is likely to be at least 3 months. The committee concluded that brigatinib for ALK-positive advanced NSCLC would likely extend life by at least 3 months.

Brigatinib meets the criteria for end-of-life treatments

3.22 The committee concluded that, although the most plausible estimate of life expectancy for people with previously treated ALK-positive advanced NSCLC was close to 24 months, the potential life extension benefit of

brigatinib was proportionally substantial. It was therefore satisfied that brigatinib met the criteria for end-of-life treatments.

Innovation

The benefits of brigatinib are adequately captured in the model

3.23 The company considered brigatinib to be innovative because it offers meaningful extension to life and improvement in progression-free life. The clinical experts explained that brigatinib has a lower toxicity than ceritinib and so is better tolerated. They said that brigatinib treatment is not a step change but is innovative because it is well tolerated at the expected dose. The committee agreed that the benefits of brigatinib over ceritinib in the central nervous system were adequately captured in the analysis through health-related quality of life. It concluded that although brigatinib may be innovative, it had not been presented with any additional evidence of benefits that were not captured in the economic model and resulting cost-effectiveness estimates.

Conclusion

Brigatinib is not recommended for people with ALK-positive advanced NSCLC

3.24 The committee considered all of the available evidence for brigatinib compared with ceritinib. It concluded that brigatinib was not a cost-effective use of NHS resources for ALK-positive advanced NSCLC after crizotinib, so it was not recommended for routine use.

Cancer Drugs Fund

Brigatinib is not recommended for use in the Cancer Drugs Fund

3.25 Having concluded that brigatinib cannot be recommended for routine NHS use, the committee considered whether it could be recommended for ALK-positive advanced NSCLC after crizotinib within the Cancer Drugs Fund. It 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. The company did not express an interest in brigatinib being considered for funding through the Cancer Drugs Fund. The committee did not acknowledge any possibility that the clinical uncertainty could be addressed through collection of data from patients having brigatinib treatment through the Cancer Drugs Fund. It therefore did not recommend brigatinib for use within the Cancer Drugs Fund as an option for people with ALK-positive advanced NSCLC who have had treatment with crizotinib.

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
July 2018

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.

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.

Emily Eaton Turner
Technical Lead

Christian Griffiths
Technical Adviser

Kate Moore
Project Manager

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