

**NATIONAL INSTITUTE FOR HEALTH AND CARE
EXCELLENCE**

Appraisal consultation document

**Atezolizumab for treating locally advanced or
metastatic non-small-cell lung cancer after
chemotherapy**

The Department of Health has asked the National Institute for Health and Care Excellence (NICE) to produce guidance on using atezolizumab 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?

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 determination.
- Subject to any appeal by consultees, the final appraisal determination may be used as the basis for NICE's guidance on using atezolizumab 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: 1 November 2017

Third appraisal committee meeting: 9 November 2017

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

1 Recommendations

- 1.1 Atezolizumab is not recommended, for treating locally advanced or metastatic non-small-cell lung cancer in adults after chemotherapy (and after targeted treatment if they have an epidermal growth factor receptor [EGFR] or anaplastic lymphoma kinase [ALK]-positive tumour mutations).
- 1.2 This recommendation is not intended to affect treatment with atezolizumab 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

Other treatments for non-small-cell lung cancer after chemotherapy include docetaxel alone, nintedanib plus docetaxel (for tumours with adenocarcinoma histology) or pembrolizumab (for tumours expressing PD-L1).

Clinical trial evidence shows that people having atezolizumab live longer than those having docetaxel alone. There is no evidence directly comparing atezolizumab with nintedanib plus docetaxel or with pembrolizumab, and indirect analyses show that any survival benefit for atezolizumab compared with these treatments is uncertain.

Atezolizumab, when compared with docetaxel alone, meets NICE's criteria to be considered a life-extending treatment at the end of life. However, it does not meet both criteria when compared with nintedanib plus docetaxel because it does not offer a proven extension to life of more than 3 months when compared with nintedanib plus docetaxel.

The most plausible cost-effectiveness estimates for atezolizumab compared with nintedanib plus docetaxel are higher than those NICE normally considers an

acceptable use of NHS resources. The cost-effectiveness estimates for atezolizumab compared with docetaxel alone are higher than those NICE normally considers acceptable for end-of-life treatments. Cost-minimisation results for atezolizumab compared with pembrolizumab are not suitable for decision-making, because clinical equivalence for atezolizumab compared with pembrolizumab has not been proven.

No cost-effectiveness estimates were provided for the subgroup of people with non-small-cell lung cancer expressing the PD-L1 protein, so no recommendations can be made for this population.

Atezolizumab is not recommended because of the high cost-effectiveness estimates compared with docetaxel and nintedanib plus docetaxel. It could not be recommended in the Cancer Drugs Fund because it does not have the plausible potential to be cost effective in these groups. No recommendations can be made for people with NSCLC expressing the PD-L1 protein.

2 The technology

Atezolizumab (Tecentriq, Roche)	
Marketing authorisation	Atezolizumab has a marketing authorisation in the UK for 'adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) after prior chemotherapy. Patients with EGFR activating mutations or ALK-positive tumour mutations should also have received targeted therapy before receiving atezolizumab.'
Recommended dose and schedule	1,200 mg every 3 weeks by intravenous infusion. The company submission states that patients should have treatment until loss of clinical benefit or unmanageable toxicity.
Price	A 1,200 mg vial costs £3,807.69 excluding VAT (company submission). The company has agreed a patient access scheme with the Department of Health. If atezolizumab had been recommended, this scheme would provide a simple discount to the list price of atezolizumab 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 administrative burden on the NHS.

3 Committee discussion

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

The condition

Atezolizumab is a potentially important option for people with locally advanced or metastatic NSCLC after chemotherapy

- 3.1 Locally advanced or metastatic non-small-cell lung cancer (NSCLC) that has progressed after chemotherapy is often diagnosed late in life and has a poor prognosis. It is a debilitating condition with many distressing symptoms. The current outlook for patients with NSCLC whose disease has relapsed after chemotherapy is poor. The clinical experts stated that people with this disease have limited treatment options, which are all associated with high toxicity. The committee noted that improving quality of life and even small extensions to life are of considerable importance to this patient group. The committee concluded that atezolizumab is a potentially important treatment option for people with locally advanced or metastatic NSCLC after chemotherapy.

Current treatments

Options for NSCLC after chemotherapy include docetaxel, nintedanib plus docetaxel, and pembrolizumab

- 3.2 Platinum therapy is given as a first treatment for NSCLC in people whose tumours are not epidermal growth factor receptor tyrosine kinase (EGFR-TK)-positive, followed by docetaxel, or nintedanib plus docetaxel for people with adenocarcinoma. For people with EGFR-TK-positive tumours, treatment starts with a tyrosine kinase inhibitor followed by platinum therapy. For people with anaplastic lymphoma kinase (ALK)-positive tumours, standard treatment is platinum combination therapy followed by an ALK inhibitor. NICE technology appraisal guidance recommends [pembrolizumab](#) for treating PD-L1-positive NSCLC after chemotherapy, [pembrolizumab](#) is also recommended for use within the Cancer Drugs Fund as an option for untreated PD-L1-positive NSCLC. The clinical experts stated that since publication of this guidance the use of

pembrolizumab has been increasing and PD-L1 testing at the point of diagnosis has become standard care for this population. The committee understood that most patients would have active treatment such as pembrolizumab, docetaxel or nintedanib plus docetaxel (for adenocarcinoma). But in a small proportion of patients who decline docetaxel, or cannot not tolerate it, best supportive care may be the only option. The committee concluded that atezolizumab could be a treatment option for people after previous chemotherapy with or without a targeted therapy and as an alternative to docetaxel, nintedanib plus docetaxel, or pembrolizumab for PD-L1-positive NSCLC.

Comparators

Docetaxel, docetaxel plus nintedanib (for adenocarcinoma) and pembrolizumab (for PD-L1-positive disease) are relevant comparators

3.3 For both second- and third-line treatment, the comparators would be docetaxel alone, nintedanib plus docetaxel (for people with adenocarcinoma), pembrolizumab (for PD-L1-positive NSCLC), and best supportive care when docetaxel is not suitable. The company had included both docetaxel and nintedanib plus docetaxel as comparators in the submission, which was appropriate. Comments received during consultation stated that nintedanib plus docetaxel is only used for a small number of people in clinical practice, but the committee considered that this was still a relevant treatment option. The company had not considered nivolumab and best supportive care, which were included in the final scope. The committee considered that excluding best supportive care was reasonable because patients eligible to have atezolizumab would be fit enough to have other treatment, and it noted that nivolumab is being appraised by NICE. The committee concluded that for the populations under consideration, the relevant comparators for this appraisal were docetaxel, nintedanib plus docetaxel for adenocarcinoma, and pembrolizumab for PD-L1-positive disease.

Clinical evidence

Atezolizumab offers a gain in survival compared with docetaxel alone

3.4 The only direct clinical trial evidence for atezolizumab compared with docetaxel came from the OAK trial. This was an open-label, phase III randomised controlled trial in adults with locally advanced or metastatic NSCLC, whose disease had progressed during or after 1 platinum-containing chemotherapy regimen. The analyses were from a primary population (n=850) and the study had recruited more patients in total (n=1,225) by the time the company made its original submission. The results showed a statistically significant median overall survival gain for atezolizumab (13.8 months; 95% confidence interval [CI] 11.8 to 15.7) compared with docetaxel (9.6 months; 95% CI 8.6 to 11.2). The committee considered that this was an important extension-to-life benefit for people with advanced NSCLC after chemotherapy. In the OAK trial, 5% of patients having atezolizumab and 17% of patients having docetaxel went on to have subsequent therapy, mostly nivolumab. In response to consultation, the company provided analyses that adjusted for this subsequent treatment. These analyses used the rank-preserving structural failure time method, which the ERG stated was not suitable for adjusting for subsequent therapies (it is normally used to adjust for treatment crossover). Therefore the committee agreed that it would use the estimates from the unadjusted trial data. The committee concluded that the unadjusted data in the company's original submission should be considered for decision-making, and that atezolizumab offers a gain in survival compared with docetaxel alone in the full population.

PD-L1 expression

Atezolizumab is more effective than docetaxel regardless of PD-L1 expression and it becomes more effective as PD-L1 expression rises

3.5 The marketing authorisation for atezolizumab is for adults with locally advanced or metastatic NSCLC after chemotherapy, and after chemotherapy and targeted treatment in people with EGFR- or ALK-positive tumours; it does not specify treatment based on PD-L1 expression. Although the company submission did not include data on all of the PD-L1 subgroups from the OAK trial, the committee noted that the trial results suggested that higher levels of PD-L1 expression led to greater clinical response in people with locally advanced or metastatic NSCLC after previous therapy (see table 1). Comments from consultation stated that it was inappropriate to make a recommendation based on PD-L1 expression because PD-L1 is not a perfect biomarker and atezolizumab has shown benefit regardless of PD-L1 expression. The committee agreed that atezolizumab is more effective than docetaxel regardless of PD-L1 expression and it also seems to become more effective as PD-L1 expression rises.

Table 1 OAK overall survival results by PD-L1 expression

Population	Number (and proportion, %)	Median overall survival (months)		Hazard ratio (95% CI)
		Atezolizumab	Docetaxel	
ITT	850 (100)	13.8	9.6	0.73 (0.62 to 0.87)
TC3 or IC3	137 (16)	20.5	8.9	0.41 (0.27 to 0.64)
TC2/3 or IC2/3	265 (31)	16.3	10.8	0.67 (0.49 to 0.90)
TC1/2/3 or IC1/2/3	463 (54)	15.7	10.3	0.74 (0.58 to 0.93)
TC0 and IC0	379 (45)	12.6	8.9	0.75 (0.59 to 0.96)

Abbreviations: CI, confidence interval; IC, tumour infiltrating immune cell; ITT, intention to treat; TC, tumour cell.

In the OAK trial, PD-L1 expression was measured using an immunohistochemistry assay. The results were grouped according to the proportion of cells stained at any intensity: TC3: ≥50%; TC2/3: ≥5%; TC1/2/3: ≥1%; TC0: <1%; IC3: ≥10%; IC2/3: ≥5%; IC1/2/3: ≥1%; IC0: <1%.

The committee was disappointed that results were not presented by PD-L1 subgroups

3.6 The company noted that response to atezolizumab was statistically significantly better than response to docetaxel alone regardless of PD-L1 expression, so it had positioned atezolizumab as a treatment for the whole population. The clinical experts agreed that therapies such as atezolizumab have shown benefit in people with both PD-L1-positive and -negative NSCLC. Further research is needed to develop tests that can be used alongside PD-L1 testing to determine which patients benefit most from treatments. Nevertheless, although PD-L1 is not a perfect biomarker, the committee considered it to be a reasonable guide as to those who may benefit from targeted treatment. The company did not provide analyses by PD-L1 expression because the trials for atezolizumab (OAK) and pembrolizumab (KEYNOTE-010) used different PD-L1 tests. The committee considered comments from a clinical expert noting that data presented at the European Society For Medical Oncology conference suggest that there is some concordance between the Ventana SP142 and

the Dako 22C3 immunohistochemistry assays. The clinical expert noted that in clinical practice it was likely that tumours identified by the 2 tests would be treated in a similar way, and there would be considerable overlap in the patients identified by the different tests as having PD-L1-positive NSCLC. Furthermore, PD-L1 testing is already established in clinical practice and, if needed, existing tests such as DAKO 22C3 could be used to inform treatment with atezolizumab. The Cancer Drugs Fund clinical lead noted that there were studies ongoing to assess the test accuracy of 4 PD-L1 assays. The committee concluded that a comparison in people with PD-L1-positive NSCLC as defined by the tests would be appropriate, given that there was likely overlap in the patients identified. Consequently, it was disappointed that the company did not present clinical and cost-effectiveness results for all of the relevant PD-L1 subgroups (including TC3 or IC3 and TC2/3 or IC 2/3, see table 1).

Indirect treatment comparisons

The overall survival results of the indirect treatment comparisons are uncertain for nintedanib plus docetaxel and pembrolizumab

3.7 In response to consultation, the company provided updated indirect treatment comparison analyses using a smaller network of comparators:

- atezolizumab (in the total population)
- docetaxel (in the total population)
- nintedanib plus docetaxel (in people with adenocarcinoma histology)
- pembrolizumab (in people with PD-L1-positive NSCLC [1% expression or more]).

The original network included comparators: atezolizumab, docetaxel, nintedanib plus docetaxel, erlotinib, pemetrexed, afatinib, gefitinib, paclitaxel and dacomitinib. The ERG stated that the results were not robust: there was statistical heterogeneity that was influenced by a range of factors, including the choice of comparators included in the network, the

populations used, use of fixed effects or random effects models, and the type of fractional polynomial model chosen. The ERG noted that the heterogeneity was such that atezolizumab may not increase overall survival compared with nintedanib plus docetaxel. The analysis estimated a difference in overall survival for atezolizumab (whole population) compared with nintedanib plus docetaxel (in people with adenocarcinoma) of 3.33 months (95% CI -0.15 to 6.81). The committee considered that the confidence intervals of the company's estimates were wide, even for a fixed effects model, and that they would be even more uncertain if a random effects model were used. The indirect treatment comparison estimated a difference in overall survival for atezolizumab (whole population) compared with pembrolizumab (PD-L1 expression $\geq 1\%$) of -0.18 months (95% CI -5.58 to 4.60). The company stated that atezolizumab could be considered clinically equivalent to pembrolizumab and that the results from the indirect treatment comparison should be considered conservative, because the populations were not equivalent and the benefits of atezolizumab for people with PD-L1-positive NSCLC may be underestimated. The committee agreed to use the company's updated network, but noted the uncertainty associated with all the indirect analyses. It could not conclude with any certainty that atezolizumab is clinically equivalent to pembrolizumab.

The company's economic model

The model structure is appropriate

- 3.8 The committee discussed the company's cost-effectiveness evidence and its critique by the ERG. It accepted the structure of the company's economic model and considered it appropriate for decision-making.

The committee accepted the corrections made in the company's updated economic model

3.9 The ERG explained that it corrected for 3 errors in the company's economic model:

- applying a different discount rate for the intervention (discount from week 1) than for the comparators (discount from year 2)
- not applying an age-related utility decrement
- applying an inappropriate half cycle correction.

In response to consultation, the company provided an updated model incorporating the ERG's corrections and an updated patient access scheme. The committee accepted the corrections made to the company's economic model.

Continued treatment effect

A lifetime treatment effect for atezolizumab is implausible

3.10 The company explained that atezolizumab's mechanism of action suggests that its effects on tumours would continue after treatment stopped. The committee considered this assumption to be biologically plausible, but it was concerned about the lack of evidence to support this. In response to consultation, the company provided updated data from the OAK trial which showed that the median length of treatment effect had increased from 16.3 months to 23.9 months. It also provided scenario analyses using various cut-offs for treatment effect, including a waning effect and spanning 5 to 20 years after stopping atezolizumab. The committee considered that the treatment effect was unlikely to last more than 5 years after treatment had stopped. It concluded that although it was biologically plausible for treatment effects to continue after stopping treatment, the length of any continued effect was uncertain.

Extrapolation of overall survival

Using a log-logistic model creates an implausibly long survival tail; Kaplan–Meier data plus an exponential curve remains optimistic

3.11 To estimate overall survival for atezolizumab, the company used data from OAK in which the median length of overall survival was 21.4 months for atezolizumab. In response to consultation, the company used Kaplan–Meier data and extrapolated the data using a log-logistic curve based on best statistical fit. The plausibility of the log-logistic model was assessed by a company advisory board of clinical experts, which stated that it was ‘not implausible’ for 10% of patients to be alive at 5 years. The company explained that its advisory board had assessed the suitability of the extrapolation based on overall outcomes. The committee considered that other options also appeared to be a good fit to the data, including the Weibull curve, and noted that the advisory board had not been presented with any other survival curves. The company also presented data on 2-, 3- and 5-year overall survival to support the overall survival outcomes in its economic model. The ERG clarified that data were provided from the POPLAR study for atezolizumab; the committee considered that the available data supported the model projections, but that these were only available up to 3 years. Data were also provided from trials for nivolumab and pembrolizumab, but the committee noted that the generalisability of these results to atezolizumab was unclear as they are different immunotherapies. The committee concluded that the log-logistic curve produced implausibly optimistic long-term survival outcomes at 5 years (10% alive). The ERG’s preferred method was to use Kaplan–Meier data up to 19 months and then extrapolate using an exponential curve, which was the best fit visually for the trial data after 19 months. The committee considered that this also produced optimistic long-term survival outcomes at 5 years (4% alive) but that these were clinically plausible. The

committee concluded that the Kaplan–Meier data with an exponential curve was appropriate for decision-making purposes.

The difference in overall survival between atezolizumab and nintedanib plus docetaxel is uncertain

3.12 The ERG recalled its earlier conclusion that atezolizumab may not provide additional clinical benefit when compared with nintedanib plus docetaxel (section 3.6) and explained that its preferred assumption was that atezolizumab did not provide an increase in overall survival compared with nintedanib plus docetaxel. However, the committee considered additional ERG analyses which varied the assumptions for overall survival, specifically:

- using the company's preferred result from the indirect treatment comparison (overall survival gain for atezolizumab of 2.65 months) and
- using the hazard ratio from the LUME-LUNG 1 trial for nintedanib plus docetaxel (overall survival gain for atezolizumab of 2.16 months).

The ERG explained that these analyses were not robust; the full range of scenarios showing the statistical heterogeneity for the company's indirect treatment comparison had not been explored so the results may be imprecise and proportional hazards did not hold for the LUME-LUNG 1 trial data. The committee concluded that the overall survival gain for atezolizumab compared with nintedanib plus docetaxel was likely to be between 0 and 2.65 months, but that these analyses were uncertain.

The committee was disappointed that cost effectiveness analyses were not presented by PD-L1 subgroup

3.13 The company did not provide cost-effectiveness analyses by PD-L1 subgroup compared with the relevant comparators (docetaxel, nintedanib plus docetaxel and pembrolizumab). The company explained that any

cost-effectiveness estimates by PD-L1 subgroup would be even more uncertain than the estimates for the whole population because atezolizumab has shown benefit in people with both PD-L1-positive and PD-L1-negative tumours. The committee discussed the PD-L1 subgroup results and noted that the hazard ratio for some subgroups, particularly the TC3 IC3 group (which represents the highest proportion of PD-L1 expression; 0.41 [0.27, 0.64]), were much lower than the TC1/2/3 or IC1/2/3 group (which represents all PD-L1 expressers; 0.74 [0.58, 0.93]). The committee was disappointed that the cost-effectiveness analyses were not presented by subgroup.

Stopping rule

The committee would have preferred a 2-year stopping rule in the model

3.14 The company explained that the evidence for immunotherapy treatments such as atezolizumab was immature, and there are no clear data demonstrating that patients are not benefiting from further treatment in the absence of disease progression, therefore patients should have treatment until they no longer clinically benefit. The committee heard from the company that there was an ongoing study investigating the effect of a 1-year maximum treatment length, the interim results of which showed that patients who discontinued therapy after 1 year had statistically significantly worse progression-free survival than those who continued therapy until they no longer benefited clinically. The committee noted that the mean length of therapy in the OAK trial was less than 11 cycles (about 33 weeks), and that there was no maximum length of treatment (that is, a stopping rule). The committee heard from the Cancer Drugs Fund clinical lead that the long-term consequences of stopping treatment are unknown, but clinical experience of immunotherapies in other indications suggests that significant treatment-related toxicities may occur while the disease is still responding. There is growing concern among clinicians about the use of immunotherapies beyond 2 years. They explained that the best length

of treatment with immunotherapies such as atezolizumab is uncertain, with clinicians stopping treatment anywhere between 6 months and 2 years. The committee considered that in some cases treatment may continue beyond 2 years, but it acknowledged that there was very limited evidence to support this. The committee understood that applying a stopping rule would reduce the costs associated with atezolizumab and could therefore improve its cost effectiveness. However, it was aware that the summary of product characteristics does not include a 2-year stopping rule and it queried whether clinicians would follow such a rule, especially if the patient was still benefiting from the treatment. The Cancer Drugs Fund clinical lead clarified that a 2-year stopping rule is acceptable to both patients and clinicians, and would be implementable. Having determined this, the committee concluded that it would have liked to have seen a 2-year stopping rule applied in the economic model.

Cost-minimisation analyses

The company's cost-minimisation estimates for atezolizumab compared with pembrolizumab are not suitable for decision-making

3.15 In response to consultation, the company provided cost-minimisation analyses comparing atezolizumab (in the total population) with pembrolizumab (in people with PD-L1-positive NSCLC expression $\geq 1\%$), on the basis that atezolizumab is clinically equivalent to pembrolizumab. The analysis showed that the overall cost for atezolizumab might be higher or lower than the cost of pembrolizumab, when taking into account the updated confidential patient access schemes for pembrolizumab and atezolizumab. The committee recalled its earlier conclusion that the survival benefit for atezolizumab compared with pembrolizumab was uncertain (section **Error! Reference source not found.**9), so concluded that the results of these analyses were not suitable for decision-making.

Cost-effectiveness estimates

There is a wide range of ICERs because of uncertainties in the data and analyses

3.16 The incremental cost-effectiveness ratios (ICERs) for atezolizumab compared with docetaxel alone are reported based on the list price for atezolizumab (ICERs including the updated patient access scheme for atezolizumab are commercial in confidence and cannot be reported here).

- The company's deterministic base-case ICER for atezolizumab compared with docetaxel alone was £91,142 per quality-adjusted life year (QALY) gained.
- The ERG's preferred deterministic ICER for atezolizumab compared with docetaxel alone was £170,497 per QALY gained.

The ICERs for atezolizumab compared with nintedanib plus docetaxel include the patient access schemes for both atezolizumab and nintedanib. (These ICERs are commercial in confidence and the exact values cannot be reported here).

- The company's deterministic base-case ICER for atezolizumab compared with nintedanib plus docetaxel was more than £30,000 per QALY gained.
- The ERG's preferred deterministic ICER for atezolizumab compared with nintedanib plus docetaxel was more than £400,000 per QALY gained.

The committee recalled that the company's probabilistic ICERs were generally about £4,000 per QALY gained higher than the deterministic ICERs, so the ERG's probabilistic ICERs were also likely to be higher than the deterministic ICERs. The committee concluded that the most plausible ICERs were likely between the company's and the ERG's base-case estimates.

The most plausible ICERs using the committee's preferred assumptions are high

3.17 The committee's preferred assumptions were:

- overall survival for atezolizumab was estimated from Kaplan–Meier data up to week 83, followed by extrapolation of trial data using an exponential model (section 3.13)
- the overall survival gain for atezolizumab compared with nintedanib plus docetaxel was likely to be between 0 and 2.65 months (section 3.14).

3.18 The committee considered that the most plausible ICERs were:

- between £91,142 and £170,497 per QALY gained for atezolizumab compared with docetaxel alone (based on the list price for atezolizumab; the ICER using the updated patient access scheme is confidential and cannot be reported here)
- between £50,000 and £100,000 per QALY gained for atezolizumab compared with nintedanib plus docetaxel (the exact ICERs are confidential and cannot be reported here).

End of life

People with NSCLC have a life expectancy of less than 24 months

3.19 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 committee discussed whether life expectancy without atezolizumab would be less than 24 months. It noted the evidence presented by the company, which showed that people with NSCLC have an average life expectancy of less than 24 months (median survival was 7.5 months for stage IIIb and 3.4 months for stage IV NSCLC). The committee concluded that the short life expectancy criterion was met.

Atezolizumab compared with docetaxel meets NICE's end-of-life criteria

3.20 The committee discussed whether a survival benefit of over 3 months can be expected for atezolizumab compared with docetaxel. The committee heard that the average number of months of life gained with atezolizumab, as estimated by the company's economic model, is 3.5 months compared with docetaxel. It agreed that there was significant uncertainty in the overall survival gain. However, the committee considered it reasonable to assume that the benefit is likely to exceed 3 months and concluded that atezolizumab met the end-of-life criteria for this population.

Atezolizumab compared with nintedanib plus docetaxel does not meet NICE's end-of-life criteria

3.21 The committee discussed whether a survival benefit of over 3 months can be expected for atezolizumab compared with docetaxel plus nintedanib in people with adenocarcinoma histology. The average number of months of life gained with atezolizumab, as estimated by the company's economic model, is 2.7 months compared with nintedanib plus docetaxel. The ERG considered that the size of the survival gain for atezolizumab was uncertain because there was no statistically significant difference in overall survival in the indirect analysis (3.33 months [95% CI -0.16 to 6.74]), and therefore it assumed that the survival gain was the same for atezolizumab and nintedanib plus docetaxel. The committee considered that the overall survival gain estimated by the company was not objective or robust and concluded that atezolizumab compared with nintedanib plus docetaxel did not offer a proven extension to life of more than 3 months.

Cancer Drugs Fund

3.22 Having concluded that atezolizumab could not be recommended for routine use, the committee then considered if it could be recommended for treating locally advanced or metastatic NSCLC after chemotherapy within 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](#). The committee understood that the company had not made a case for atezolizumab to be considered for funding through the Cancer Drugs Fund. It also considered that the most plausible ICERs were substantially higher than the range normally considered to be a cost-effective use of NHS resources. The committee therefore concluded that atezolizumab did not have plausible potential to satisfy the criteria for routine use, and that there were no clinical uncertainties that could be resolved through data collection within the Cancer Drugs Fund.

- 3.23 The committee concluded that atezolizumab did not meet the criteria to be considered for inclusion in the Cancer Drugs Fund. It did not recommend atezolizumab for use within the Cancer Drugs Fund as an option for people with locally advanced or metastatic NSCLC after chemotherapy.

Conclusion

Atezolizumab is not recommended

- 3.24 The committee concluded that the most plausible ICERs for the whole population irrespective of PD-L1 expression (see section 3.17) were higher than those usually considered a cost-effective use of NHS resources, even for end-of-life treatments. The cost-effectiveness evidence was highly uncertain for atezolizumab compared with nintedanib plus docetaxel. Moreover, the clinical equivalence of atezolizumab compared with pembrolizumab was highly uncertain and therefore the results of the cost-minimisation analyses were not suitable for decision-making. The committee was unable to make a judgement on the cost effectiveness of atezolizumab for people who have PD-L1-positive NSCLC, because cost-effectiveness estimates were not provided for this subgroup. The committee concluded that it could not recommend atezolizumab as an option for routine use or within the Cancer Drugs

Fund for locally advanced or metastatic NSCLC after chemotherapy in adults.

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.

Peter Selby

Chair, appraisal committee

October 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 C](#).

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.

Jessica Maloney

Technical lead

Fay McCracken

Technical adviser

Stephanie Yates

Project manager

ISBN: [to be added at publication]