Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2492

atezolizumab 840mg and 1,200mg concentrate for solution for infusion (Tecentriq®)

Roche Products Ltd

08 July 2022

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

ADVICE: following a full submission

atezolizumab (Tecentriq®) is accepted for use within NHSScotland.

Indication under review: as monotherapy as adjuvant treatment following complete resection for adult patients with Stage II to IIIA (7th edition of the UICC/AJCC staging system) non-small cell lung cancer (NSCLC) whose tumours have PD-L1 expression on ≥50% of tumour cells and whose disease has not progressed following platinum-based adjuvant chemotherapy.

In an open-label, randomised, phase III study, disease-free survival in patients with stage II to IIIA NSCLC, was significantly longer in patients whose tumours had PD-L1 expression on ≥1% of tumour cells and numerically longer in patients whose tumours had PD-L1 expression on ≥50% of tumour cells with atezolizumab compared with best supportive care. All patients prior to randomisation had disease that had not progressed following adjuvant platinum-based chemotherapy, following complete resection.

This SMC advice takes account of the benefits of a Patient Access Scheme (PAS) that improves the cost-effectiveness of atezolizumab. This advice is contingent upon the continuing availability of the PAS in NHS Scotland or a list price that is equivalent or lower.

Chairman
Scottish Medicines Consortium

Indication

As monotherapy as adjuvant treatment following complete resection for adult patients with Stage II to IIIA (7th edition of the UICC/AJCC staging system) non-small cell lung cancer (NSCLC) whose tumours have PD-L1 expression on ≥50% of tumour cells and whose disease has not progressed following platinum-based adjuvant chemotherapy.[1]

Dosing Information

The recommended dose of atezolizumab administered intravenous infusion is either 840mg every 2 weeks, 1,200mg every 3 weeks or 1,680mg every 4 weeks. Treatment is continued for one year unless there is disease recurrence or unacceptable toxicity.

Dose reductions are not recommended. The Summary of Product Characteristics (SPC) provides advice on the management of adverse events.

Patients should be selected for treatment based on the tumour expression of PD-L1 confirmed by a validated test.

Atezolizumab must be initiated and supervised by physicians experienced in the treatment of cancer.[1]

Product availability date

27 January 2022

Atezolizumab received an Innovation Passport allowing entry into the Medicines and Healthcare Products Regulatory Agency Innovative Licensing and Access Pathway on 2 August 2021.

Summary of evidence on comparative efficacy

Atezolizumab is a humanised monoclonal antibody that binds to programmed death-ligand 1 (PD-L1) and blocks its interactions with the programmed death-1 (PD-1) and B7.1 receptors on tumour cells and tumour infiltrating immune cells. This prevents PD-L1/PD-1 mediated inhibition of the immune response, including reactivating the anti-tumour immune response without inducing antibody-dependent cellular cytotoxicity.[1]

Evidence comes from the open-label, randomised, phase III study (IMpower010) which compared adjuvant atezolizumab with best supportive care (BSC) in adult patients with early NSCLC. Eligible patients were aged ≥18 years with stage IB (tumours ≥4cm) to IIIA non-small cell lung cancer (NSCLC) (according to the 7th edition of the Union for International Cancer Control [UICC] / American Joint Committee on Cancer [AJCC] staging system). They had complete resection of NSCLC in the 28 to 84 days before enrolment and an Eastern Co-operative Oncology Group (ECOG) performance status of 0 or 1. They completed up to four cycles of cisplatin-based chemotherapy (investigator's choice of cisplatin plus vinorelbine, docetaxel, gemcitabine or pemetrexed). Then, 3

to 8 weeks after the last dose of chemotherapy, 1,005 eligible patients were randomised equally to receive atezolizumab (1,200mg by intravenous infusion every 3 weeks) or BSC (observation and regular scans for disease recurrence) for 16 cycles or until disease progression or unacceptable toxicity. Randomisation was stratified according to sex, stage of the disease (stage IB or stage II or stage IIIA), histology (squamous or non-squamous) and level of PD-L1 expression. Crossover from BSC to atezolizumab was not allowed.[2]

The primary outcome was investigator-assessed disease-free survival (DFS; defined as the time from randomisation to date of occurrence of first documented disease recurrence, new primary NSCLC or death due to any cause, whichever occurred first). The study used a hierarchical statistical testing strategy for the primary and secondary outcome (overall survival) with no formal testing of outcomes after the first non-significant outcome in the hierarchy. The hierarchical order was the primary outcome assessed firstly in patients with stage II to IIIA NSCLC with PD-L1 expression on ≥1% of tumour cells; secondly in patients with stage II to IIIA NSCLC and thirdly in the intention-to-treat (ITT) population (all randomised patients, that is, in IB to IIIA population) and finally the secondary outcome (overall survival) in the ITT population.[2]

At the interim analysis of DFS, at data cut-off of January 2021 after a median follow up of approximately 32 months, atezolizumab significantly improved DFS compared with BSC in subpopulations of patients with stage II to IIIA NSCLC with PD-L1 expression on ≥1% of tumour cells and with stage II to IIIA NSCLC regardless of PD-L1 expression. The difference in DFS between atezolizumab and BSC did not reach the pre-specified DFS interim analysis boundary for statistical significance in the ITT population and there was no further formal testing. Therefore the results reported for these outcomes are descriptive only and non-inferential (no p-values reported). At the time of the interim DFS analysis, median overall survival had not been reached in either group. Results are presented in Table 1.[2]

Table 1: Results for the primary and secondary outcomes of IMpower010.[2]

	Atezolizumab	**BSC**	**Stratified hazard ratio (95% CI), p-value**
Primary outcome: investigator assessed DFS			
Patients with stage II to IIIA NSCLC and PD-L1 ≥1%	**n=248**	**n=228**	
Patients with DFS event	88	105	
Median DFS, months	NE	35.3	0.66 (0.50 to 0.88), p=0.0039
3-year DFS rate	60%	48%	
Patients with stage II to IIIA NSCLC	**n=442**	**n=440**	
Patients with DFS event	173	198	
Median DFS, months	42.3	35.3	0.79 (0.64 to 0.96), p=0.020
3-year DFS rate	56%	49%	
Patients with stage IB to IIIA NSCLC (ITT)	**n=507**	**n=498**	
Patients with DFS event	187	212	

Median DFS, months	NE	37.2	0.81 (0.67 to 0.99), p=NS
3-year DFS rate	58%	53%	
Secondary outcome: overall survival in ITT population			
Patient deaths	97	90	
Median overall survival	NE	NE	1.07 (0.80 to 1.42)

BSC=best supportive care; CI=confidence interval; ITT=intention-to-treat; NSCLC=non-small cell lung cancer; PD-L1= programmed death-ligand 1; DFS=disease-free survival: NE=not evaluable; NS=not significant

Investigator-assessed DFS was analysed as a secondary outcome in the patients with stage II to IIIA NSCLC whose tumours expressed PD-L1 on ≥50% of tumour cells. This subgroup of patients (n=229) reflects the licensed population. Median DFS was longer in patients in the atezolizumab group compared with the BSC group but since this outcome was not included in the hierarchical testing, results were considered descriptive only; see table 2 for details. Death had occurred in 16% of patients in this subgroup and overall survival data were immature. Exploratory analysis of overall survival suggested a trend favouring atezolizumab over BSC; unstratified hazard ratio 0.37 (95% confidence interval [CI]: 0.18 to 0.74).[1,3]

Table 2: Results for the outcome of investigator-assessed DFS in patients with stage II to IIIA NSCLC and PD-L1 ≥50% of tumour cells (January 2021 data cut-off).[1,3]

	Atezolizumab	**BSC**	**Unstratified hazard ratio (95% CI)**
	n=115	**n=114**	
Median duration of follow-up, months	34.2		
Patients with DFS event	28	52	
Median DFS, months	NE	35.7	0.43 (0.27 to 0.68)
3-year DFS rate	74%	49%	

BSC=best supportive care; CI=confidence interval; NSCLC=non-small cell lung cancer; PD-L1= programmed death-ligand 1; DFS=disease-free survival: NE=not evaluable

Quality of life outcomes were not assessed during IMpower010.[2]

The company performed post hoc analyses of the licensed subpopulation of the IMpower010 study excluding the small number of patients with epidermal growth factor receptor (*EGFR*) and anaplastic lymphoma kinase (*ALK*) mutations. At the data cut-off of January 2021, the median DFS in the atezolizumab subgroup (n=106) was not reached compared with 37.3 months in the BSC group (n=103); HR 0.43 (95% CI: 0.26 to 0.71). This was similar to results in the licensed subpopulation.[4,5]

Summary of evidence on comparative safety

In the safety population of IMpower010 study (n=990) at data cut-off 21 January 2021, patients had received a median of 16 cycles of atezolizumab and 65% (323/495) of patients completed 16 cycles of atezolizumab. Any treatment-emergent adverse event (AE) was reported by 93% (459/495) of patients in the atezolizumab group and 71% (350/495) in the BSC group and these

were considered treatment-related in 68% in atezolizumab group. In the atezolizumab and BSC groups respectively, patients reporting a grade 3 or 4 AE were 22% versus 12% and patients with a reported serious AE were 18% versus 8.5%. In the atezolizumab group, 29% of patients had an AEs that led to dose interruptions and 18% of patients discontinued therapy due to an AE.[2]

The most frequently reported treatment-emergent AEs of any grade in the atezolizumab group (n=495) versus BSC group (n=495) included immune-mediated AEs of rash (18% versus 2.2%), hepatitis (17% versus 4.4%), hypothyroidism (17% versus 0.6%), hyperthyroidism (6.5% versus 0.8%) and pneumonitis (3.8% versus 0.6%) and other AEs of cough (13% versus 9.3%), pyrexia (13% versus 2.2%), arthralgia (11% versus 5.3%), pruritus (10% versus 0.6%) and nasopharyngitis (6.7% versus 10%). In the atezolizumab group (n=495), the most frequently reported treatment-related AEs were hypothyroidism (11%), pruritus (8.7%), rash (8.1%), increased aspartate aminotransferase (7.5%), increased alanine aminotransferase (7.3%), hyperthyroidism (5.9%), pyrexia (5.5%) and arthralgia (5.3%). Immune-mediated AEs required treatment with systemic corticosteroids in 12% and 0.8% of patients respectively.[2]

There were four deaths in the atezolizumab group that were considered related to atezolizumab or chemotherapy: one each due to interstitial lung disease, multiple organ dysfunction syndrome, myocarditis and acute myeloid leukaemia.[2]

Safety in the licensed population (patients with stage II to IIIA NSCLC with PD-L1 expression on ≥50% of tumour cells) was reported to be consistent with the overall study population and the known safety of atezolizumab.[3]

Summary of clinical effectiveness issues

Lung cancer is the most common type of cancer in Scotland and NSCLC accounts for approximately 80% to 85% of cases. In 2020 in Scotland, 47% of lung cancer cases were diagnosed at stage IV (metastatic) with a further 20% at stage III (locally advanced); therefore only approximately 30% of patients were diagnosed at an early stage (I or II). For patients who present with early NSCLC, stage I and II and selected IIIA, surgery with curative intent may be an option for suitable patients who are well enough. Guidelines recommend adjuvant chemotherapy for patients with resected stage II and III NSCLC, taking account of performance status, comorbidities, time from surgery and recovery; for patients with stage IIA disease, adjuvant chemotherapy is recommended for those whose resected tumours were >4cm. Three or four cycles with cisplatin-based combination chemotherapy mainly with vinorelbine but also with gemcitabine, docetaxel or pemetrexed (only for adenocarcinomas) is recommended. Despite the use of adjuvant chemotherapy, recurrence rates remain high and the survival benefits are modest. The 5-year survival rates for early NSCLC remain poor: 55% of patients with stage I, 35% with stage II and 15% with stage III.[2,6-9]

Recently, the EGFR inhibitor, osimertinib, has been licensed as adjuvant treatment after complete resection, for patients with stage IB to IIIA NSCLC, whose tumours have *EGFR* exon 19 deletions or exon 21 L858R substitution mutations. However there are currently no other treatment options for patients without EGFR mutations and these patients undergo active surveillance after completing adjuvant chemotherapy.[4]

Key strengths

- Atezolizumab is the first immunotherapy to be licensed for adjuvant treatment in patients with early NSCLC after complete resection and adjuvant chemotherapy. It is licensed for use in patients with stage II to IIIA disease and in those whose tumours have PD-L1 expression on ≥50% of tumour cells.[1]
- Available results from the IMpower010 study have indicated significantly improved DFS in patients with stage II to IIIA disease with PD-L1 expression on ≥1% of tumour cells (stratified HR of 0.66) and numerically improved DFS (unstratified HR of 0.43) in those with PD-L1 expression on ≥50% of tumour cells. The larger DFS improvement in patients with PD-L1 expression on ≥50% of tumour cells was considered clinically meaningful and represents the patients who would be eligible for treatment under the marketing authorisation.[1,2]
- Since osimertinib has recently been licensed for early adjuvant treatment after complete tumour resection in patients with NSCLC whose tumours have *EGFR* mutations and other targeted adjuvant therapy is being studied in patients with *ALK* mutations, the submitting company acknowledged that atezolizumab would not be the treatment of choice for these patients. In post hoc analysis, the treatment effect was similar (unstratified HR of 0.43 in those with PD-L1 expression on ≥50% of tumour cells) when patients with *EGFR* or *ALK* mutations, who may receive alternative targeted adjuvant treatment in the future, were excluded from the analysis.[5]
- The safety profile of atezolizumab in this patient population was consistent with that of other atezolizumab monotherapy studies.[2]

Key uncertainties

- A subpopulation of 23% of the IMpower010 study population represented the licensed indication. DFS was assessed as a secondary outcome in the licensed population but since this was not controlled for multiplicity, the results are considered descriptive only.[2]
- Since there was no significant difference between atezolizumab and BSC for DFS in the ITT population, there was no formal testing of overall survival.[2]
- At the data cut-off (January 2021), overall survival had not been reached in the atezolizumab group. Longer term results are awaited to confirm overall survival benefits. Results may be affected by an imbalance in the use of subsequent, post-progression immunotherapy (3.7% versus 13% of atezolizumab and BSC groups in the ITT population respectively).[1,2]
- Quality of life was not assessed during the IMpower010 study and it is uncertain if the addition of adjuvant atezolizumab would have a detrimental effect on patients' quality of life in early disease.[2]

Companion diagnostic required: contact local laboratory for information**.**

Summary of comparative health economic evidence

The submitting company provided a cost-utility analysis for atezolizumab, capturing the full licenced treatment population. Within the model, 1,200mg atezolizumab was administered every three weeks for up to 16 cycles (around 11 months). Patients receiving atezolizumab were compared to those receiving BSC, which was defined as observation and regular scans for disease reoccurrence.

The model used a Markov structure, comprising of seven health states and an absorbing death state. Over the time horizon of 40 years, patients could move through the disease pathway of disease free, locoregional recurrence, first line metastatic recurrence and second line metastatic recurrence. At each recurrence stage, patients were further subdivided between those receiving treatment and those not receiving treatment.

The main source of clinical evidence used in the model was from the IMpower010 study.[2] This source informed the occupancy of the disease free state over time and the probability of moving from the disease free state to a recurrence state or death. The model used parametric survival curves to project the duration of DFS beyond the period observed in the study. The company stated that the observed period within the study was not representative of long-term outcomes for patients, and so made a series of adjustments to the projections, setting a minimum value for the mortality rate, assuming a proportion of patients would be cured over time and limiting the duration of the atezolizumab treatment effect to 5 years.

The IMpower010 study did not capture the outcomes of patients after they experienced a recurrence. As a result, the probabilities of all subsequent movements in the model were informed by a selection of papers identified in the literature.

Similarly, no health related quality of life was captured in the IMpower010 study. Utility values for each of the health states were taken from the literature. To account for differences in age and gender between the source and the modelled populations, each source value was transformed into a disutility, relative to the age and gender adjusted value from the general population. This disutility was then applied to patients within each state, using the UK age and gender adjusted general population value as a base. The resulting mean utility values ranged between 0.78 for those in the disease free- state to 0.62 for those in any of the recurrence states not in receipt of treatment.

Costs in the model include treatment with atezolizumab and subsequent lines of therapies at locoregional, first line metastatic and second line metastatic stage. Each administration of atezolizumab was assumed to be accompanied by a blood test and full clinical review. As patients progress through disease stages they were subject to increasing levels of monitoring, utilizing more care staff time (e.g. GP visits, community nurse time) and more testing (e.g. CT scans and electrocardiograms). End of life costs of £4,740 were assumed for those dying because of the cancer.

A Patient Access Scheme (PAS) was submitted by the company and assessed by the Patient Access Scheme Assessment Group (PASAG) as acceptable for implementation in NHSScotland. Under the PAS, a discount was offered on the list price. A confidential PAS is also in place for pembrolizumab, which was assumed to be used as a subsequent treatment at the metastatic first line stage.

The results presented do not take account of the PAS for pembrolizumab or the PAS for atezolizumab but these were considered in the results used for decision-making. SMC is unable to present the results provided by the company which used an estimate of the PAS price for pembrolizumab due to commercial confidentiality and competition law issues.

Table 3. Base case cost-effectiveness results – PD-L1 ≥50% Stage II–IIIA population – atezolizumab list price

Technologies	Total Life Year Gain	Incremental life year gain	ICER (£/QALY)
Atezolizumab	9.74	2.49	£20,306
BSC	7.25		

Abbreviations: BSC, best supportive care; QALY, quality adjusted life year; ICER, incremental cost effectiveness ratio

The company provided a variety of scenario analyses, a selection of which are presented below.

Table 4. Scenario analysis – PD-L1 ≥50% Stage II–IIIA population – atezolizumab list price

#	Scenario	Scenario input description	Base case input description	ICER (£/QALY)
1	DFS distributions	Exponential (lowest ICER alternative)	Log-normal	£19,580
2		Gompertz (highest ICER alternative)		£35,628
3	Treatment effect	Maintained over Time	Maintained up to 5 years	£19,763
4	Atezolizumab treatment schedule	1,680mg/ every 4 weeks	1,200mg/ every 3 weeks	£21,733
5	Allow vial sharing	No	Yes	£20,261
6	End of Life costs	Exclude	Included	£21,367
7	Time horizon	10 years	40 years	£ 35,864
8		20 years		£ 22,342
9		30 years		£ 20,403
10	Maximum "cure" proportion	20%	91.5%	£27,010
11		40%		£25,382
12		60%		£23,571
13		80%		£21,560
14	Fewer atezolizumab admin costs	Only IV cost each admin	Inclusion of clinical review and blood count at each admin	£19,082
15	Metastatic recurrence 1L treatment	100% patients pembrolizumab	Atezolizumab.: 100% pembrolizumab BSC: 50% pembrolizumab, 50% atezolizumab	£ 19,203

Abbreviations: BSC, best supportive care; QALY, quality adjusted life year; ICER, incremental cost effectiveness ratio; DFS, disease free survival

The strengths of the economic case were assessed as being:

- The comparator appeared to be appropriate and was tested against atezolizumab in a randomised controlled trial.
- The model structure was appropriate and had been informed through a systematic review and consultations with health economic and clinical experts.
- The company validated many of the clinical assumptions with UK and Scottish clinicians.
- The central results suggested that atezolizumab is highly cost effective compared to BSC. Sensitivity and scenario analysis showed that results were stable across a wide range of alternative assumptions.

The limitations of the economic case were assessed as being:

- DFS results, taken from the IMpower010 study, were not formally reviewed for statistical significance in the licensed population. This leads to uncertainty in the economic results based on these data.
- Overall survival, outcomes for patients who experienced a recurrence and health related quality of life were not captured in the IMpower010 study. This meant the model was reliant upon a complex network of alternative data sources to fill in these gaps. These external, heterogeneous sources may have left the economic case open to unknown sources of bias.
- The adjustments made to the survival functions relied on external data sources and assumptions. The company provided some explanation as to the choices made and sensitivity analysis exploring alternative assumptions, which showed only small changes in the economic results. However, these projections remain a source of some uncertainty.

After considering all the available evidence, the Committee accepted atezolizumab for use in NHSScotland.

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

Summary of patient and carer involvement

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

- We received patient group submissions from Roy Castle Lung Cancer Foundation and the Scottish Lung Cancer Nurses Forum. Roy Castle Lung Cancer Foundation is a registered charity and the Scottish Lung Cancer Nurses Forum is an unincorporated organisation.
- Roy Castle Lung Cancer Foundation has received 12.5% pharmaceutical company funding in the past two years, including from the submitting company. The Scottish Lung Cancer Nurses Forum has received 100% pharmaceutical company funding in the past two years, including from the submitting company.

- Lung cancer patients continue to have an exceptionally poor prognosis. They often suffer multiple distressing and difficult to manage symptoms such as breathlessness, weight loss, fatigue and chest pain. These symptoms can reduce their ability to carry out personal care, cook for themselves and contribute actively to family or business activities.
- There is a need for additional available treatment options which may reduce disease recurrence and improve survival rates. Little progress has been made in the adjuvant setting for over a decade.
- Improving quality of life, symptom management and even small extensions in duration of life are of considerable importance to patients and families. Atezolizumab represents an additional treatment to help improve patients' longer term survival. Any extra time is important. Continuing to monitor and manage side effects may be seen as a 'price worth paying' for some potential extra life extension. Atezolizumab is already a commonly used treatment for lung cancer and the side effect/safety profile expected to be similar in the adjuvant setting. Atezolizumab therefore potentially adds benefits for both patients and society in preventing or delaying early lung cancer recurrence, or progression to metastatic disease.

Additional information: guidelines and protocols

The Scottish Intercollegiate Guidelines Network (SIGN) published "Management of lung cancer: A national clinical guideline (SIGN 137)" in February 2014.[10] The guidance makes the following relevant recommendations:

- Patients with stage I and II NSCLC should be considered for curative surgery whenever possible.
- Patients with [stage IIIA] early N2 NSCLC may be considered for surgery as part of multimodality treatment. All of these cases must be discussed at the multidisciplinary team meeting.
- Patients with good performance status (PS 0-1) who have completely resected NSCLC (stage II to IIIA) should be offered platinum-based postoperative systemic anticancer therapy.
- Patients with NSCLC who have had complete tumour resection should not receive postoperative radiotherapy, except as part of a randomised trial.

This guidance predates the availability of osimertinib and atezolizumab for early NSCLC.

The National Institute for Health and Care Excellence (NICE) published "Lung cancer: diagnosis and management" in 2019.[7] This guidance makes the following relevant recommendations:

- Offer postoperative chemotherapy to people with good performance status (WHO 0 or 1) and T1a–4, N1–2, M0 NSCLC.
- Consider postoperative chemotherapy for people with good performance status (WHO 0 or 1) and T2b–4, N0, M0 NSCLC with tumours greater than 4 cm in diameter.
- Offer a cisplatin-based combination chemotherapy regimen for adjuvant chemotherapy.

This guidance predates the availability of osimertinib and atezolizumab for early NSCLC.

The European Society for Medical Oncology (ESMO) published "Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO clinical practice guidelines for diagnosis, treatment and follow-up" in 2017 and the guidance was subsequently updated in 2021.[8,9] The guidance makes the following relevant recommendations for stage I to IIIA disease:

- Surgery should be offered to all patients with stage I to IIIA NSCLC as the preferred treatment to all who are willing to accept procedure-related risks.
- Adjuvant chemotherapy should be offered to patients with resected TNM 8th edition stage IIB and III NSCLC and can be considered in patients with resected stage IIA disease and a primary tumour >4 cm. Pre-existing comorbidity, time from surgery and postoperative recovery need to be taken into account in this decision taken in a multidisciplinary tumour board.
- For adjuvant chemotherapy, a two-drug combination with cisplatin is preferable. In randomised studies, the attempted cumulative cisplatin dose was up to 300mg/m^2, delivered in three to four cycles. The most frequently studied regimen is cisplatin–vinorelbine and combinations such as cisplatin plus gemcitabine or docetaxel or pemetrexed (only for adenocarcinomas) could also be feasible. Carboplatin is an accepted alternative when cisplatin is not feasible. Carboplatin and paclitaxel is a potential option for stage IIA resected primary tumour >4cm.
- Osimertinib is indicated for the adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA NSCLC whose tumours have *EGFR* exon 19 deletion or exon 21 L858R substitution mutations.
- Post-operative radiotherapy in completely resected early stage I-IIIA NSCLC is not recommended.
- Patients treated with radical intent should be followed for treatment-related complications, detection of treatable relapse or occurrence of second primary lung cancer. Multidisciplinary team assessment is needed for feasibility check for treatment of locoregional relapse.
- Surveillance every 6 months for 2 years including a contrast-enhanced volume chest and abdominal CT scan at 12 and 24 months at least is recommended.

This guidance predates the availability of atezolizumab for this indication.

Additional information: comparators

Active surveillance.

Additional information: list price of medicine under review

Medicine	Dose Regimen	Cost per course (£)
Atezolizumab	840mg every 2 weeks or 1,200mg every 3 weeks or 1,680mg every 4 weeks administered by intravenous infusion for one year	64,731 to 69,300

Costs from BNF online on 10 May 2022. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take patient access schemes into consideration.

Additional information: budget impact

The submitting company estimated there would be 99 patients eligible for treatment with atezolizumab in each year to which confidential estimates of treatment uptake were applied. However, the estimated patient numbers appear to be based on treatment population of those with a PD-L1 expression greater than 1%, which is not matched to the current licenced indication. Taking into account the higher PD-L1 threshold could approximately half the treated population.

SMC is unable to publish the with PAS budget impact due to commercial in confidence issues. A budget impact template is provided in confidence to NHS health boards to enable them to estimate the predicted budget with the PAS.

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

References

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3. Felip E, Altorki N, Zhou C, Vallieres E, Vynnychenko I et al. Atezolizumab (atezo) vs best supportive care (BSC) in stage II-IIIA NSCLC with high PD-L1 expression: sub-analysis from the pivotal phase III IMpower010 study. Ann Oncol 2022; 33 (suppl2): S71 abstract 800.

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5. Zhou C, Thakur MD, Srivastava MK, Zou W, Xu H et al. IMpower010: biomarkers of disease-free survival (DFS) in a phase III study of atezolizumab (atezo) vs best supportive care (BSC) after adjuvant chemotherapy in stage IB-IIIA NSCLC. Ann Oncol 2021; 32 (suppl7): S1374 abstract 20.

6. Public Health Scotland. Cancer Incidence and Prevalence in Scotland (to December 2020). Publication date: 12 April 2022. Available at: https://publichealthscotland.scot/

7. National Institute for Health and Care Excellence (NICE). Lung cancer: diagnosis and management. 2019; Available at: https://www.nice.org.uk/guidance/ [accessed 25 April 2022]

8. Postmus PE, Kerr KM, Oudkerk M, Senan S, Walker DA et al. Early and locally advanced non-small cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017; 28 (Suppl 4): iv1-iv21.

9. Remon J, Soria J-C, Peters S on behalf of the ESMO Guidelines Committee. Early and locally advanced non-small cell lung cancer: an update of the ESMO Clinical Practice Guidelines focusing on diagnosis, staging, systemic and local therapy. Ann Oncol 2021; 32: 1637-42.

10. Scottish Intercollegiate Guidelines Network (SIGN). Management of lung cancer: A national clinical guideline (SIGN137). 2014. Available at: https://www.sign.ac.uk/ [accessed 25 April 2022]

This assessment is based on data submitted by the applicant company up to and including 17 May 2022.

**Agreement between the Association of the British Pharmaceutical Industry (ABPI) and the SMC on guidelines for the release of company data into the public domain during a health technology appraisal:*https://www.scottishmedicines.org.uk/about-us/policies-publications/

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

therefore asked to consider contract pricing when reviewing advice on medicines accepted by SMC.

Patient access schemes: A patient access scheme is a scheme proposed by a pharmaceutical company in order to improve the cost-effectiveness of a medicine and enable patients to receive access to cost-effective innovative medicines. A Patient Access Scheme Assessment Group (PASAG), established under the auspices of NHS National Services Scotland reviews and advises NHSScotland on the feasibility of proposed schemes for implementation. The PASAG operates separately from SMC in order to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHSScotland on the basis of a patient access scheme that has been considered feasible by PASAG, a set of guidance notes on the operation of the scheme will be circulated to Area Drug and Therapeutics Committees and NHS Boards prior to publication of SMC advice.

Advice context:

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

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