SMC2689

pembrolizumab concentrate for solution for infusion (Keytruda®)

Merck Sharp & Dohme UK Limited

06 September 2024

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

ADVICE: following a full submission

pembrolizumab (Keytruda®) is accepted for restricted use within NHSScotland.

Indication under review: as monotherapy for the adjuvant treatment of adults with non-small cell lung carcinoma who are at high risk of recurrence following complete resection and platinum-based chemotherapy.

SMC restriction: adults whose tumours express programmed death-ligand 1 (PD-L1) with less than 50% (0 to 49%) tumour proportion score (TPS).

In a randomised, phase III study pembrolizumab (as adjuvant therapy) was associated with statistically significant benefits in disease-free survival over placebo in patients with completely resected stage IB-IIIA non-small cell lung carcinoma.

This advice applies only in the context of an approved NHSScotland Patient Access Scheme (PAS) arrangement delivering the cost-effectiveness results upon which the decision was based, or a PAS/ list price that is equivalent or lower.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Pembrolizumab is a humanised monoclonal antibody that blocks the interaction between programmed cell death-1 (PD-1) receptor and its ligands, PD-L1 and PD-L2. This potentiates T-cell responses, including anti-tumour responses of antigen presenting cells and tumours or other cells in the tumour microenvironment. The recommended dose of pembrolizumab for this indication is 200 mg every 3 weeks or 400 mg every 6 weeks administered via intravenous infusion over 30 minutes; patients should be treated until disease recurrence, unacceptable toxicity or for a duration of up to one year.[1]

1.2. Disease background

Lung cancer is the most common cancer in Scotland and in 2021 it accounted for 16% of all cancers. The most prevalent type is non-small cell lung carcinoma (NSCLC) accounting for approximately 85% of all lung cancer cases. Most patients with lung cancer are diagnosed at an advanced stage. In Scotland in 2021, it was reported that 46% of lung cancer cases were diagnosed at stage IV, 20% at stage III and approximately 27% of patients were diagnosed at an early stage (I or II).[2, 3]

1.3. Company proposed position

Adults whose tumours express programmed death-ligand 1 (PD-L1) with less than 50% (0 to 49%) tumour proportion score (TPS).

1.4. Treatment pathway and relevant comparators

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 resectable stage IIIA NSCLC who can have surgery and are well enough for multimodality therapy, neoadjuvant chemoradiotherapy can be considered with surgery. Equivalence of neoadjuvant and adjuvant chemotherapy has been reported for overall survival.[4-6]

Recently, novel neoadjuvant and adjuvant immunotherapy treatments have been used in Scottish clinical practice for specific subgroups of early stage resected NSCLC patients. These include nivolumab in combination with platinum-based chemotherapy for the neoadjuvant treatment of resectable NSCLC (SMC2619), atezolizumab as adjuvant treatment following complete resection for adult patients with Stage II to IIIA NSCLC whose tumours have PD-L1 expression on ≥50% of tumour cells and whose disease has not progressed following platinum-based adjuvant chemotherapy (SMC2492), and osimertinib as adjuvant treatment after complete tumour resection in adult patients with stage IB-IIIA NSCLC whose tumours have epidermal growth factor receptor (EGFR) exon 19 deletions (Ex19del) or exon 21 (L858R) substitution mutations (SMC2383). There are currently no adjuvant treatment options for patients with early-stage NSCLC and PD-L1 TPS <50%, who are not EGFR mutation-positive, following complete resection and platinum-based chemotherapy; these patients at present are actively monitored.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of pembrolizumab for the adjuvant treatment of patients with completely resected stage IB-IIIA non-small cell lung carcinoma comes from KEYNOTE-091.

Table 2.1. Overview of relevant studies[3, 7]

Criteria	KEYNOTE-091
Study design	An international, randomised, triple-blind, phase III study.
Eligible patients	• Adults with pathologically confirmed NSCLC (any histology) of stage IB (tumours of ≥4 cm in diameter), II, or IIIA per the AJCC staging system (7th edition) after complete surgical resection including negative margins (R0). • Available tumour sample for PD-L1 assessment and known PD-L1 expression status. • No evidence of disease on clinical examination and radiographic assessment per RECIST version 1.1 assessed by local review after surgery but within 12 weeks before randomisation. • ECOG performance status 0 or 1
Treatments	Pembrolizumab, 200 mg every 3 weeks or placebo for up to a maximum of 18 cycles. Treatment was to continue until completion of 18 infusions, disease recurrence, unacceptable adverse events, patient withdrawal, investigator's opinion, non-compliance, or other discontinuation criteria were met.
Randomisation	Patients were randomised equally. Randomisation was stratified according to stage (IB/II/IIIA), adjuvant chemotherapy (yes/no), PD-L1 status (TPS = 0%/1-49%/≥50%), and region (Western Europe/Eastern Europe/Asia/Rest of the World).
Primary outcome	The co-primary outcomes were DFS in the overall population and in the PD-L1 TPS ≥50% population, defined as time from randomisation to locoregional or metastatic recurrence assessed per RECIST version 1.1 by investigator review, appearance of a second NSCLC primary or other malignancy, or death from any cause, whichever occurred first.
Secondary outcomes	DFS in the PD-L1 TPS of 1% or greater population; OS in the overall population, PD-L1 TPS of 50% or greater population, and PD-L1 TPS of 1% or greater population; lung cancer-specific survival in the overall population.
Statistical analysis	A graphical approach of Maurer and Bretz was used to account for multiple testing, and so if one null hypothesis was rejected, the alpha was shifted to other hypotheses. The Hwang-Shih-DeCani spending function with gamma = -4 was used to control the type I error in the interim/final analysis for each DFS and OS outcome. The subgroup of interest for this submission (prior adjuvant chemotherapy and PD-L1 TPS status <50%) were not controlled for type I error.

Abbreviations: AJCC = American Joint Committee on Cancer; DFS = disease-free survival; ECOG = Eastern Cooperative Oncology Group; NSCLC = non-small cell lung carcinoma; OS = overall survival; PD-L1 = programmed cell death ligand 1; RECIST = Response Evaluation Criteria in Solid Tumours; TPS = tumour proportion score.

In the overall study population, pembrolizumab significantly improved DFS versus placebo. At a later data-cut (interim analysis 3), DFS in the overall study population was not tested for significance however numerically favoured pembrolizumab over placebo; overall survival (OS) in the overall study population also failed to achieve statistical significance (median OS had not been reached). See Table 2.2 for more details.[3, 7]

Table 2.2. Selected key outcomes from KEYNOTE-091.[3, 7]

	Interim analysis 2 (data-cut: 20 September 2021)		Interim analysis 3 (data-cut: 24 January 2023)	
	Pembrolizumab	**Placebo**	**Pembrolizumab**	**Placebo**
Median follow-up	32.4 months		46.7 months	
Co-primary outcome: DFS in overall population (RECIST version 1.1, investigator-assessed)				
	n=590	n=587	n=590	n=587
Events	212	260	*	*
Median DFS	53.6 months	42.0 months	53.8 months	43.0 months
HR (95% CI)	0.76 (0.63 to 0.91) p=0.001		0.81 (0.68 to 0.96)	
Co-primary outcome: DFS in PD-L1 TPS ≥50% population (RECIST version 1.1, investigator-assessed)				
	n=168	n=165	n=168	n=165
Events	54	63	*	*
Median DFS	NR	NR	67.0 months	47.6 months
HR (95% CI)	0.82 (0.57 to 1.18) p=0.136		0.83 (0.59 to 1.16) p=0.135	
Secondary outcome: overall survival in overall population				
	n=590	n=587	n=590	n=587
Events	98	111	*	*
Median OS	NR	NR	NR	NR
HR (95% CI)	0.87 (0.67 to 1.15) p=0.168		0.87 (0.69 to 1.10) p=0.118	

Note: 86% of patients in the overall population had prior adjuvant chemotherapy. Abbreviations: CI = confidence interval; DFS = disease-free survival; HR = hazard ratio; OS = overall survival; NR = not reached; PD-L1 = programmed cell death ligand 1; RECIST = Response Evaluation Criteria in Solid Tumours; TPS = tumour proportion score.
*considered confidential by company.

2.2. Evidence to support the positioning proposed by the submitting company

The submitting company presented subgroup analysis from KEYNOTE-091 that are relevant to the proposed positioning, that is in patients whose tumours express PD-L1 TPS <50%. Unlike the

overall study population, all patients in this subgroup had prior adjuvant platinum-based chemotherapy as per the licensed indication. See Table 2.3 for details of the results.

Table 1.3 Selected efficacy outcomes of KEYNOTE-091 in the subgroup of patients with PD-L1 TPS <50% (interim analysis 3: data-cut 24 January 2023).[8]

	Pembrolizumab (n=363)	Placebo (n=363)
Primary outcome: DFS (RECIST version 1.1, investigator-assessed)		
Events	168	199
Median DFS	51.7 months	34.5 months
HR (95% CI)	0.72 (0.58 to 0.89)	
Secondary outcome: overall survival		
Deaths	84	110
Median OS	NR	NR
HR (95% CI)	0.73 (0.55 to 0.97)	

Abbreviations: CI = confidence interval; CPS = combined positive score; DFS = disease-free survival; HR = hazard ratio; KM = Kaplan-Meier; NR = not reached; OS = overall survival; PD-L1 = programmed death-ligand 1.

2.3. Health-related quality of life outcomes

Health-Related Quality of Life (HRQoL) was assessed using three questionnaires: Eastern Cooperative Oncology Group quality of Life questionnaire (EORTC QLQ-C30-version 3), EORTC QLQ-LC13 and EQ-5D. Quality of life scores were stable over time in both treatment groups; no meaningful changes between treatment groups were observed (patient-reported outcome full analysis set). Moreover, EQ-5D-5L data presented by the company in the subgroup of patients with PD-L1 TPS <50% showed no clinically meaningful changes from baseline in either treatment group.[3]

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

3. Summary of Safety Evidence

At data-cut 20 September 2021, the median duration of treatment was 11.7 months in the pembrolizumab group and 11.8 months in the placebo group. Any treatment-emergent adverse event (AE) was reported by 96% (556/580) of patients in the pembrolizumab group and 91% (529/581) in the placebo group and these were considered treatment-related in 75% and 52% respectively. In the pembrolizumab and placebo groups respectively, patients reporting a grade 3 or higher AE were 34% versus 26%, patients with a reported serious AE were 25% versus 15%, the proportion of AEs that led to dose interruptions were 38% versus 25% and patients discontinuing therapy due to an AE was 20% versus 5.9%.[3, 7]

In the safety population, the most frequently reported treatment-related/emergent AEs of any grade with an incidence ≥5% in the pembrolizumab group versus placebo group were: hypothyroidism (20% versus 3.3%), hyperthyroidism (9.3% versus 2.6%), pruritus (18% versus 10%), diarrhoea (13% versus 8.1%), fatigue (11% versus 9.1%), rash (6.0% versus 2.9%) and increased alanine aminotransferase (5.7% versus 4.1%). Immune-mediated AEs and infusion reactions are known AEs of special interest associated with pembrolizumab. These occurred in 39% of patients in the pembrolizumab group and 13% of patients in the placebo group, the most

common were: hypothyroidism (21%), hyperthyroidism (11%) and pneumonitis (6.9%). No new safety concerns were identified from KEYNOTE-091.[3, 7]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Evidence is available from KEYNOTE-091, a well-conducted, phase III study that compared pembrolizumab with placebo. Pembrolizumab (used for one year as adjuvant therapy) was associated with statistically significant benefits in disease-free survival over placebo in patients with completely resected stage IB-IIIA NSCLC.
- There were numerical benefits in DFS associated with pembrolizumab over placebo in patients whose tumours express PD-L1 TPS <50%. An approximate gain of 17.2 months in DFS was observed; HR = 0.72 (95% CI: 0.58 to 0.89).[8]
- The placebo treatment group in KEYNOTE-091 is a reasonable proxy for active monitoring, which is the most relevant comparator in Scottish clinical practice for patients whose tumours express PD-L1 TPS <50%.

4.2. Key uncertainties

- Although the relevant subgroup to support the positioning proposed by the submitting company was sizeable (62% of the total study population), it is not a prespecified subgroup and the study was not powered to detect differences between these treatment groups. Therefore, the results are descriptive only and should be interpreted with caution. The overall study population was wider than the licensed indication (the study included patients without prior adjuvant chemotherapy).
- Histology (squamous versus non-squamous) was not used as a stratification factor. In the PD-L1 TPS <50% subgroup, there were differences at baseline in histology between the pembrolizumab and placebo groups, which may bias results in favour of pembrolizumab.[3]
- Overall survival data are immature and have not been formally tested in the PD-L1 TPS <50% subgroup; median OS has not been reached at the latest data-cut.[3]
- There is uncertainty regarding the efficacy of pembrolizumab in patients in this setting with an EGFR/ALK mutation. More than half of the total study population (57%) had an unknown EGFR mutational status, making results difficult to interpret. Only 14 patients (1.2%) in the total study population had documented ALK positive disease and 73 patients had documented EGFR positive disease (6.2%).[3] Patients with an EGFR mutation may be unlikely to receive pembrolizumab in this setting in NHSScotland due to the availability of osimertinib (SMC2383).

4.3. Clinical expert input

Clinical experts consulted by SMC considered that pembrolizumab fills an unmet need in this therapeutic area, since patients with early-stage NSCLC and PD-L1 TPS <50%, who are not EGFR mutation-positive, do not receive active treatment at present following complete resection and platinum-based chemotherapy. They consider pembrolizumab to be a therapeutic advancement for these patients.

4.4. Service implications

The introduction of pembrolizumab for the adjuvant treatment of patients with NSCLC who are at high risk of recurrence following complete resection and platinum-based chemotherapy, who have PD-L1 TPS <50%, may impact on workload across the oncology service, including day units and pharmacy services.

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

5. Summary of Patient and Carer Involvement

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

- We received patient group submissions from the 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 7.6% pharmaceutical company funding in the past two years, including from the submitting company. The Scottish Lung Cancer Nurses Forum has not received any pharmaceutical company funding in the past two years.
- Living with lung cancer can present troublesome symptoms such as fatigue, persistent cough and shortness of breath, this in turn can have a major impact on the persons quality of life. Daily activities such as showering and dressing become exhausting for them. They may be unable to work which provides added financial strain, they may feel isolated, and everything becomes an effort. Their loved ones are also affected in coping with the physical and emotional changes, which can be very challenging. Everyone's quality of life is affected with lung cancer.
- Apart from adjuvant chemotherapy after surgery, there is currently no added adjuvant immunotherapy treatment for those who have PD-L1 TPS <50%. Having access to adjuvant pembrolizumab has the potential to delay or prevent recurrence and potentially provide extension of life. This would have substantial benefits for both the patient and wider society.
- Pembrolizumab is already a commonly used treatment for lung cancer and no new safety concerns are expected in this setting. A six weekly dosing interval may be preferrable for patients.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

The economic analysis is summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost utility analysis
Time horizon	36.5 years – based on the mean starting age in KEYNOTE-091
Population	Adults with NSCLC who are at high risk of recurrence following complete resection and platinum-based chemotherapy and whose tumours express PD-L1 with less than 50% (0-49%) tumour proportion score.
Comparators	Active Monitoring is the most relevant comparator in this sub population, as the company and SMC clinical experts agree that osimertinib is only available to patients with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations.
Model description	A four-state Markov model was used. The included states were disease free (DF), local-regional recurrence (LR), distant metastasis (DM) and death. All patients entered the model in the DF state before transitioning to subsequent states. The death state could be reached from any state. The cycle length was 1 week with a half cycle correction applied.
Clinical data	The main source of clinical evidence for pembrolizumab and active monitoring (placebo) arms was the KEYNOTE-091 study. No indirect treatment comparison was required in this submission.
Extrapolation	For the transitions from the DF state to LR and DM, the pembrolizumab and placebo arms were fitted separately with log-normal survival curves to the KEYNOTE-091 data. For the transitions from DF to death state, an exponential function was used. The KEYNOTE-091 study did not routinely collect data on further progression once patients experienced local-regional recurrence as their first event. Therefore, transitions from the LR state to DM or death were estimated by applying exponential functions from the real-world SEER-Medicare database[9]. These transitions were applied uniformly across the treatment arms. Transitions from the DM state were dependent upon the assumed first-line treatment for metastatic NSCLC. The proportions of subsequent treatments were based on clinical expert opinion, and overall survival (OS) was estimated from external sources. The company applied an adjustment factor which increased the DM mortality rate in the model, to correct for prognostic differences between the SEER-Medicare cohort (as applied in the model) and the patients in the clinical studies. The model is set up to assume no ongoing benefit from exposure to pembrolizumab in the adjuvant setting. A calibration of downstream transitions to fit observed OS in the KEYNOTE-091 study was applied, as the modelled pembrolizumab arm was underpredicting observed OS. The submitting company temporarily calibrated all three transitions at once (LR-DM, LR-death, DM-death) as it produced good visual fit to the OS curves. A cure assumption was included where between 5-7 years the per-cycle risk of progression (movement to both LRR and DM) from the disease-free state is reduced linearly by 95%. A calibration cap is also tapered linearly from 5-7 years to match the cure assumption.
Quality of life	EQ-5D-3L data were collected as part of the KEYNOTE-091 study. The utility values used are: 0.852 for DF, 0.776 for LR, and 0.743 for DM pre-progression substate. Grade 1 and 2 adverse events were not included in the DF utility value. The submitting company sourced a utility value for the DM post-progression substate from pooling KEYNOTE-407[10] and KEYNOTE-189[11] to get a utility value of 0.668. This was because there was insufficient data in the KEYNOTE-091 study to generate a utility value for this substate. Adverse events grade 3+ were included as a one-off disutility and were estimated from KEYNOTE-091 study.
Costs and resource use	Medicine costs included in the model were for acquisition costs (for pembrolizumab and subsequent treatments), administration costs and adverse events costs. The model included the costs of salvage surgery and radiotherapy in the LR states. Additionally, hospitalisation costs, outpatient visits, consultations with nurses, GPs and

	occupational therapists, monitoring (CT scans, chest radiography and ECG) and end of life costs were included.
PAS	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.

6.2. Results

The main base case results are presented in Table 6.2.

Table 6.2. Base-case results, with PAS

Technologies	Total LYs	Incremental LYs	ICER vs. comparator (£/QALY)
Pembrolizumab	9.09	-	
Placebo	7.99	1.10	£21,599

Abbreviations: ICER, incremental cost-effectiveness ratio; LYG, life years gained; QALYs, quality-adjusted life years

Disaggregated results show that the main cost differences between pembrolizumab and active monitoring is the adjuvant treatment costs associated with pembrolizumab, which are slightly offset by the subsequent treatment costs in the distant metastasis state. The main source of higher quality adjusted life years in the pembrolizumab arm was the longer duration spent in the disease-free state.

6.3. Sensitivity analyses

To explore areas of uncertainty the company conducted deterministic sensitivity analysis and probabilistic sensitivity analysis. These analyses suggested that the main drivers of the economic results were the exponential rates of OS and PFS failure for metastatic NSCLC treatments, utility value in the disease-free state, and unit cost of IV medicine administration.

A selection of scenarios is presented in Table 6.3

Table 6.3. results of scenario analyses and justifications, with PAS

No	Base case	Scenario	ICER vs. comparator (£/QALY)
		Base-case	£21,599
1	Cure point 5-7 years	Cure point 5 years	£21,204
2		Cure point 5-10 years	£22,296
3	Calibration cap 5-7 years	Calibration cap 6-8 years	£21,426
4	Calibration and SEER adjustment included	Calibration removed entirely	£23,857
5		Calibration removed, SEER adjustment added	£24,147
6		Calibration without SEER adjustment	£21,761

7		Calibration applied to all TPs except for I/O ineligible subpopulation	£20,392
8	Pembrolizumab given Q3W	Pembrolizumab given Q6W	£20,708
9	Log-normal/log-normal DFS curves (DF-LR/DF-DM)	Weibull/log-normal DFS curves	£23,758
10		Log-logistic/log-normal DFS curves	£22,301
11	40% of DM on no active treatment in 1L	20% of DM patients on no active treatment in 1L	£24,184
12	Assume 15% receive targeted therapies	Assume 5% receive targeted therapies	£20,664
13	DF utilities excluded grade1-2 AEs	DF utilities including g1-2- AEs	£22,999

Abbreviations: ICER = incremental cost effectiveness ratio, QALY = quality adjusted life years, DFS = disease-free survival, DF = disease free, LR = local/regional recurrence, DM = distant metastasis, SEER = Surveillance, Epidemiology, and End Results program, HSUV = health state utility values, 1L = first line, AEs = adverse events.

6.4. Key strengths

- The economic analysis matches the proposed positioning.
- The model structure appears appropriate and is similar to other SMC submissions.
- The main source of clinical data is taken from KEYNOTE-091, a phase III randomised placebo-controlled study.
- Utility values were estimated from EQ-5D data in the KEYNOTE-091 study.

6.5. Key uncertainties

- Transitions from the Local-regional Recurrence (LR) health state and Distant Metastasis (DM) health state were sourced using external data. For example, LR transitions were estimated from SEER-Medicare databases, and the DM to death transitions were based on expert opinion (for the proportions of subsequent treatment options) and external clinical study data. However, the sources used seemed reasonable and the company provided adequate sensitivity analyses, which showed minimal variations in the ICER estimates.
- There is inherent uncertainty when extrapolating survival data. While other plausible distributions choices could increase the ICER, the company's use of log-normal distributions for the Disease-Free (DF) transitions to LR and DM states is methodologically sound.
- The submitting company performed a calibration on modelled OS since the initial model, which assumed no ongoing benefit to pembrolizumab, underpredicted the observed overall survival in the pembrolizumab arm. This introduces uncertainty because the calibration relied on immature observed OS data from the KEYNOTE-091 study. However, multiple scenario analyses were performed for this uncertainty and showed only modest variation in the ICER estimates.
- The utility values for the DF health state appears slightly high compared to an age matched

general population cohort, particularly for patients aged 70+. However, scenario analysis using a lower utility value suggested that this may not be a significant driver of economic results.

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

7. Conclusion

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

8. Guidelines and Protocols

Scottish Intercollegiate Guidelines Network (SIGN). SIGN 134. Management of lung cancer.[4]

National Institute for Health and Care Excellence (NICE). NICE guideline [NG122]. Lung cancer: diagnosis and management.[5]

Early and locally advanced non-small-cell lung cancer (NSCLC): ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.[6]

9. Additional Information

9.1. Product availability date

18 December 2023

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per 1-year course
pembrolizumab	**200 mg every 3 weeks or 400 mg every 6 weeks administered via intravenous infusion; patients should be treated until disease recurrence, unacceptable toxicity or for a duration of up to one year.**	**£94,680**

Costs from BNF online on 01 July 2024. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs assume dosing schedule of 400 mg every 6 weeks for one year. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The submitting company estimated there would be 23 patients treated with pembrolizumab in year 1 rising to 24 in year 5.

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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8. Msd. Data on File. KEYNOTE-091 IA3 Statistical Report.

This assessment is based on data submitted by the applicant company up to and including 16 August 2024.

**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.