Healthcare Improvement Scotland | SMC Advice on new medicines

SMC2907

pembrolizumab concentrate for solution for infusion (Keytruda®)

Merck Sharp & Dohme (UK) Limited

07 August 2026

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 use within NHSScotland.

Indication under review: as monotherapy for the treatment of resectable locally advanced head and neck squamous cell carcinoma as neoadjuvant treatment, continued as adjuvant treatment in combination with radiation therapy with or without concomitant cisplatin and then as monotherapy in adults whose tumours express PD-L1 with a CPS≥ 1.

Evidence from an open-label phase III study demonstrated that the addition of perioperative pembrolizumab to adjuvant radiotherapy, with or without cisplatin, improved event-free survival. Adjuvant radiotherapy, with or without cisplatin, is the most relevant comparator in this setting.

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 monoclonal antibody which binds to the programmed cell death-1 (PD-1) receptor and blocks its interaction with the programmed cell death-ligand 1 (PD-L1). Some cancers produce PD-L1 which combines with PD-1 to switch off activity of certain cells of the immune system, preventing them from attacking the cancer. By blocking PD-1, pembrolizumab increases the immune system's ability to kill the cancer cells.[1, 2]

For the neoadjuvant and adjuvant treatment of resectable locally advanced head and neck squamous cell carcinoma (HNSCC), patients should be treated with neoadjuvant pembrolizumab as monotherapy for two doses of 200 mg by intravenous infusion (IV) every 3 weeks or one dose of 400 mg or until disease progression that precludes definitive surgery or unacceptable toxicity, followed by adjuvant treatment with pembrolizumab in combination with radiation with or without concomitant cisplatin for three doses of 200 mg every 3 weeks or two doses of 400 mg every 6 weeks followed by pembrolizumab as monotherapy for 12 doses of 200 mg every 3 weeks or six doses of 400 mg every 6 weeks or until disease recurrence or unacceptable toxicity. Subcutaneous pembrolizumab has also been recently licensed for the neoadjuvant and adjuvant treatment of resectable locally advanced HNSCC. For more information, see Summary of Product Characteristics (SPC).[1]

1.2. Disease background

HNSCC are an anatomically heterogeneous group of cancers including tumours originating in the lip, oral cavity, pharynx, larynx, paranasal sinuses or salivary glands; the most common sites are the lip and oral cavity (42%).[3] Nasopharyngeal, sinonasal and salivary gland cancers are usually considered distinct from typical HNSCC and are managed differently. Around 75% to 85% of HNSCC is due to tobacco use and alcohol consumption, although human papillomavirus (HPV) infection as a cause of oropharyngeal cancer is increasing.[4] Younger and healthier individuals have higher rates of HPV-associated cancer than tobacco-associated cancers and these patients generally have a better prognosis. Symptoms of HNSCC include chronic pain in the throat, persistent hoarseness and sore tongue, or non-healing ulcers or red/white patches in the mouth, painful or difficulty swallowing and neck masses.[4] Approximately 50% of patients with HNSCC are diagnosed at the locally advanced stage, and the 5-year overall survival rate of resectable locally advanced HNSCC is around 40 to 50%.[3]

1.3. Treatment pathway and relevant comparators

The well-established standard of care treatment for locally advanced resectable HNSCC is surgical resection of the tumour, followed by adjuvant radiotherapy alone or in combination with chemotherapy in high-risk patients (such as patients with extra nodal extension and/or positive resection margins). The most common chemotherapy treatment used in this setting is cisplatin.[5-7] There is no Cancer Medicines Outcomes Programme Public Health Scotland real-world evidence report for this submission.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of pembrolizumab in combination with adjuvant radiotherapy with or without cisplatin for the treatment of locally advanced resectable HNSCC comes from KEYNOTE-689. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant study

Criteria	KEYNOTE-689[3, 8]	
Study design	Multicentre, randomised, open-label, phase III study.	

Eligible patients	• Adult patients with newly diagnosed, non-metastatic, resectable locally advanced HNSCC with (AJCC Staging Manual, 8th edition):
	  ○ stage III oropharyngeal p16-positive disease with tumour size T4 and node stage N0 to N2 or
	  ○ stage III or IVA oropharyngeal p16-negative disease or
	  ○ stage III or IVA laryngeal, hypopharyngeal or oral cavity disease independent of p16 status.
	• ECOG performance status 0 or 1.
	• Eligible for primary surgery.
	• Evaluable tumour burden based on RECIST 1.1 criteria.	

Treatments	Pembrolizumab plus SoC:
	• Neoadjuvant pembrolizumab, 200 mg IV every 3 weeks for 2 cycles.
	• Surgery
	• Adjuvant treatment:
	  ○ Pembrolizumab 200 mg IV every 3 weeks for 3 cycles
	  ○ Radiotherapy
	  ○ Cisplatin 100 mg/m^2 BSA IV every 3 weeks for 3 cycles (high-risk patients only)
	• Pembrolizumab monotherapy 200 mg IV every 3 weeks as maintenance for 12 cycles.
		SoC:
		• No neoadjuvant treatment.
		• Surgery
		• Adjuvant treatment:
		  ○ Radiotherapy
		  ○ Cisplatin 100 mg/m^2 BSA IV every 3 weeks for 3 cycles (high-risk patients only)

	Treatment continued until disease progression (verified by BICR), initiation of a new anticancer treatment, pregnancy, death, withdrawal of consent, study conclusion or early termination, whichever occurs first. A participant only discontinued from neoadjuvant treatment if disease progression precluded surgery.	
Randomisation	Patients were randomised equally. Randomisation was stratified according to primary tumour site (oropharynx or oral cavity versus larynx versus hypopharynx), tumour stage (III versus IVA), and PD-L1 status according to centrally determined TPS (≥50% versus <50%).	
Primary outcome	EFS assessed by BICR according to RECIST, version 1.1, defined as the time from randomisation to radiographic disease progression occurring during the neoadjuvant phase and preventing surgery, local or distant progression or recurrence on imaging or biopsy, or death from any cause.	
Secondary outcomes	mPR (defined as ≤10% invasive squamous cell carcinoma within the resected primary tumour specimen and all sampled regional lymph nodes) and OS (defined as time from the date of randomisation to the date of death due to any cause).	
Statistical analysis	Efficacy analyses were performed in the CPS≥10 population, the CPS≥1 population, and the ITT population, which included all randomised patients. The study was	

	powered to detect differences in EFS, mPR, and OS and overall type I error was controlled at alpha = 2.5% using the Mauer and Bretz graphical approach.

Abbreviations: AJCC = American Joint Committee on Cancer; BICR = blinded independent central review; BSA = body surface area; CPS = combined positive score; ECOG = Eastern Cooperative Oncology Group; EFS = event-free survival; HNSCC = head and neck squamous cell carcinoma; HPV = human papillomavirus; IV = intravenous; mPR = major pathological response; OS = overall survival; PD-L1 = programmed cell death-ligand-1; RECIST 1.1 = Response Evaluation Criteria in Solid Tumours version 1.1; SoC = standard of care; TPS = tumour proportion score

The addition of perioperative pembrolizumab to standard of care significantly improved event-free survival (EFS) in patients with locally advanced HNSCC whose tumours express PD-L1 with a combined positive score (CPS) ≥ 1. Statistical significance was also reached for the key secondary outcome major pathological response (mPR); overall survival (OS) was not formally tested in the PD-L1 CPS ≥1 subgroup. *See Table* 2.2 for details.

Table 2.2. Key efficacy results for KEYNOTE-689 (data-cut: 25 July 2024) (licensed population – PD-L1 CPS ≥ 1).[3]

	Pembrolizumab + SoC (n=347)	SoC (n=335)
Primary outcome: event-free survival (BICR, as per RECIST 1.1 criteria)		
Events, n	128	156
Median EFS	59.7 months	29.6 months
Hazard ratio (95% CI)	0.70 (0.55 to 0.89) p=0.0014	
EFS rate at 12 months	75%	61%
Key secondary outcome: major pathological response		
Number of mPR	34	0
mPR rate	9.8%	0%
p-value	<0.001	
Key secondary outcome: overall survival		
Events, n	106	128
Median OS	NR	61.8 months
Hazard ratio (95% CI)	0.72 (0.56 to 0.94)	
OS rate at 6 months	94%	88%

Abbreviations: BICR = Blinded independent central review; CI = Confidence interval; CPS = Combined positive score; EFS = Event-free survival; HR = Hazard ratio; mPR = major pathological response; NR = not reached; OS = Overall survival; RECIST 1.1 = Response Evaluation Criteria in Solid Tumours Version 1.1; SoC = standard of care

2.2. Health-related quality of life outcomes

Health-Related Quality of Life was assessed using European Organisation for Research and Treatment of Cancer Quality of Life questionnaire (EORTC QLQ)-C30, EORTC QLQ-H&N35, and EQ-5D-5L. Overall, quality of life and symptom scores remained stable in the neoadjuvant treatment phase, and mean changes from baseline were generally similar between the pembrolizumab plus standard of care and standard of care groups in the post adjuvant treatment phase (where both groups received radiotherapy plus or minus cisplatin [Week 25 to Week 51]).[3, 9]

3. Summary of Safety Evidence

Evidence from KEYNOTE-689 supports the relative safety of the addition of pembrolizumab to standard of care for the treatment of patients with resectable locally advanced HNSCC. The control group of KEYNOTE-689 can be considered representative of the most relevant comparator

in this setting. Data are presented from the first interim analysis (data-cut 25 July 2024); median time on study treatment was 9.1 months and 2.9 months in the pembrolizumab plus standard of care and standard of care groups respectively.[3]

In the pembrolizumab plus standard of care and standard of care groups respectively (all participants as treated [APaT] population), 96% (348/361) and 97% (305/315) had one or more adverse events (AEs), of which 81% and 82% were considered treatment-related; 76% and 74% had a grade 3 to 5 AE, of which 45% and 43% were considered treatment-related; 50% and 37% had a serious AE; 24% and 14% discontinued treatment due to an AE; 1.1% and 0.3% died due to a treatment-related AE.[3] The most commonly reported AEs considered related to treatment with incidence >10% were radiation skin injury (39% versus 47%), stomatitis (39% versus 52%), hypothyroidism (19% versus 1.9%), fatigue (18% versus 13%), nausea (18% versus 21%), dry mouth (18% versus 22%), dysgeusia (13% versus 18%), neutrophil count decreased (12% versus 19%), lymphocyte decreased (11% versus 8.9%), vomiting (11% versus 7.9%), white blood cell count decreased (11% versus 16%), dysphagia (10% versus 16%), weight decreased (9.7% versus 11%), anaemia (8.9% versus 11%).[3]

Overall, the safety profile of pembrolizumab when combined with standard of care (adjuvant radiotherapy with or without cisplatin) is considered clinically acceptable. AEs reported in KEYNOTE-689 were in line with what has previously been reported for the individual components, and no new safety signals or excess toxicity were recorded.[3] Patients receiving pembrolizumab should be monitored for infusion-related reactions and immune-mediated AEs.[1]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Pembrolizumab is the first immunotherapy to be licensed as monotherapy for the treatment of resectable locally advanced HNSCC as neoadjuvant treatment, continued as adjuvant treatment in combination with radiotherapy with or without concomitant cisplatin and then as monotherapy in adults whose tumours express PD-L1 with a CPS ≥ 1.
- KEYNOTE-689 provides direct evidence versus the most relevant comparator in practice (adjuvant radiotherapy with or without cisplatin).
- The addition of perioperative pembrolizumab to standard of care significantly improved EFS; the 30% reduction in risk of EFS (HR 0.70, 95% CI: 0.55 to 0.89, p=0.0014) in the PD-L1 CPS ≥ 1 subgroup can be considered clinically meaningful. EFS sensitivity analysis were overall consistent with the primary analysis.[3] Neoadjuvant pembrolizumab did not reduce the proportion of patients who underwent curative surgery.
- Early indications suggest that pembrolizumab may have a benefit in OS in the PD-L1 CPS ≥ 1 subgroup (HR 0.72 95% CI: 0.56 to 0.94).[3, 8]

4.2. Key uncertainties

- The EFS treatment effect reported in KEYNOTE-689 is likely overestimated due to methodological limitations. EFS assessment started later in the pembrolizumab group compared with the control group because patients received neoadjuvant pembrolizumab whereas patients in the control group had immediate surgery. The median difference at first efficacy assessment was 3.7 weeks, which was maintained in subsequent efficacy assessments. There were late changes to the study protocol definition of EFS, such that disease progression during the neoadjuvant phase that did not preclude surgery was excluded as an event, which may have also contributed to overestimation of treatment effect.[3]
- There were some limitations with the OS data. In the PD-L1 CPS ≥ 1 population, OS was not formally tested and therefore results are descriptive only. Furthermore, OS data are not mature; events have occurred in approximately 35% of the study population. Further data are awaited.[3, 8]
- KEYNOTE-689 was an open-label study, and therefore outcomes such as patient-reported quality of life should be interpreted cautiously.
- Although mPR was associated with statistically significant improvements, the extent to which mPR predicts long-term clinical benefit in this setting is uncertain.[3]
- The number of patients with HPV-positive tumours was lower than what has been reported in other studies of HNSCC. In KEYNOTE-689, 3.8% had HPV-positive tumours compared with studies in advanced/metastatic HNSCC (KEYNOTE-048 = 22%; KEYNOTE-040 = 24%). This is likely due to the high proportion of patients with non-oropharyngeal cancer (approximately 90%) in KEYNOTE-689 as well as the restricted eligibility criteria based on HPV status.[3]

4.3 Clinical expert input

Clinical experts consulted by SMC considered that pembrolizumab fills an unmet need and is a therapeutic advancement for the treatment of resectable locally advanced HNSCC.

4.4 Service implications

There may be service implications associated with the introduction of pembrolizumab for this indication. Patients in this setting are not currently tested for PD-L1 status, and pembrolizumab is administered in addition to current standard of care, meaning that additional resource will be required for the prescribing, administration and monitoring (blood tests and imaging) of pembrolizumab.

Diagnostic test required to identify patients eligible for treatment: contact local laboratory for information.

5 Summary of Patient and Carer Involvement

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

- We received a patient group submission from Head and Neck Cancer UK (HANCUK), which is a registered charity.
- HANCUK has not received any pharmaceutical company funding in the past two years.
- Head and neck cancer is a term describing several conditions, each with its own effects and potential outcomes for patients with the disease. Dependent upon the type of cancer, patients can suffer long-term facial disfigurement, an inability to eat or speak which leads to a loss of confidence and isolation. The mental considerations of living with head and neck cancer and the effects upon the sufferer and their immediate family is considerable.
- The principle of shrinking tumours prior to surgery should result in a reduction in the severity of the surgery and a consequential improved recovery time. This could lead to a reduction in the care needs of the patient and a benefit to their immediate family.
- Whilst the treatment to shrink tumours before surgery is becoming more common, it is imperative that the treatment does not have a detrimental effect on the patient's quality of life. Quality of life should be the overriding consideration. Potential side effects should be considered alongside measures to prevent or minimise them.

6 Summary of Comparative Health Economic Evidence

6.3 Economic case

The economic case is summarised in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis.
Time horizon	A lifetime time horizon of 40 years.
Population	Adult (18 years or older) patients newly diagnosed with resectable stage III-IVa locally advanced HNSCC who have PD-L1 CPS≥1.
Comparators	The comparator was standard of care (SoC). SoC consisted of surgical resection followed by adjuvant radiotherapy plus cisplatin for patients with high-risk pathological features or radiotherapy alone for patients without high-risk pathological features.
Model description	A Markov model was used, which contained four mutually exclusive health states; event-free (EF), local or salvageable recurrence (L/SR), incurable recurrence/progression (IRP), and death. All patients entered the model in the EF health state receiving either perioperative pembrolizumab plus SoC or SoC. From the EF state, patients could transition to the L/SR, IRP, or death states. In the L/SR state, patients could receive salvage surgery, radiotherapy or systemic oncologic therapy, and could transition to IRP or death. In the IRP state, patients were assumed to receive first-line therapy for recurrent/metastatic HNSCC and could also receive second-line therapy in this setting. The IRP health state was separated into pre- and post-progression sub-states.

Clinical data	The main source of clinical evidence was patient-level data from KEYNOTE-689 (data-cut, 25th July 2024).[3, 8]
Extrapolation	Transition probabilities from the event-free (EF) state were estimated using parametric survival models fitted to individual patient-level data from the KEYNOTE-689 study, following a multistate modelling approach.[10, 11] Separate parametric extrapolations were fitted for each EF transition (EF to L/SR, EF to IRP, and EF to death), with competing risks accounted for within the modelling framework. Gompertz, Gompertz, and generalised gamma distributions were selected for the EF to L/SR, EF to IRP, and EF to death transitions, respectively. Transitions from the L/SR and IRP health states were modelled using exponential functions.
Quality of life	EQ-5D data from KEYNOTE-689 were used to derive health state utility values for the EF, L/SR, IRP (pre-progression) states. A utility decrement for grade 3 and above AEs was calculated from these data. Literature values were used to estimate a health state utility value for IRP (post-progression). Utilities were age adjusted.
Costs and resource use	Costs included medicine acquisition, administration, initial surgery and adjuvant radiotherapy, AEs, subsequent treatments (including radiotherapy, salvage surgery and systemic therapy), disease management (by health state), PD-L1 testing and terminal care.
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 of was offered on the list price. A PAS discount is in place for nivolumab and this was included in the results used for decision-making by using estimates of the comparator PAS price.

6.4 Results

The base case economic analysis concluded that the use of pembrolizumab was associated with increased costs but also improved health outcomes. The scale of those health outcomes was estimated to be 1.28 incremental quality adjusted life years.

SMC considered results for decision-making that took into account all relevant PAS. SMC is unable to present these results due to competition law issues.

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

6.5 Sensitivity analyses

A range of sensitivity analyses were presented. Key descriptions of the scenario analysis are provided in Table 6.3.

Table 6.3: Scenario analysis

	Parameter	Base case	Scenario	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
	Base case			*CiC*	1.28	*CiC*
1a	EF transitions (EF→L/SR/ IRP/ death)	Parametric: Gompertz/ Gompertz/ Gen gamma	Parametric: Gen gamma/ Gen gamma/ Gen gamma	*CiC*	1.73	*CiC*
1b			Parametric: Log normal/ Gompertz/ Gen gamma	*CiC*	1.00	*CiC*
2	Cure point	Excluded	Applied at 5 years (from EF)	*CiC*	1.26	*CiC*
3	Censoring rule from EF state	EFS rule (last disease assessment)	OS rule (last known date alive)	*CiC*	1.12	*CiC*
4	IRP post-progression utility	EXTREME	KEYNOTE-689 pre-progression IRP utility	*CiC*	1.26	*CiC*

5	Pembrolizumab dosing (adjuvant)	200 mg Q3W for 1 dose, followed by 400 mg Q6W for up to 7 cycles	200 mg Q3W for up to 15 cycles	*CiC*	1.28	*CiC*
6	Vial sharing	Permitted	Not permitted	*CiC*	1.28	*CiC*
7	Systemic treatment in L/SR state	KEYNOTE-689 (L/SR)	KEYNOTE-689 (1L IRP)	*CiC*	1.28	*CiC*
8	1L treatment for IRP (SoC arm)	SoC arm: Nivolumab included	SoC arm: Nivolumab redistributed to pembrolizumab monotherapy	*CiC*	1.28	*CiC*
9	Rechallenge with PD-L1 (IRP state)	Excluded	Included	*CiC*	1.28	*CiC*
10a	Time horizon	Lifetime (40.1 years)	20 years	*CiC*	1.05	*CiC*
10b			30 years	*CiC*	1.25	*CiC*
11	Initial surgery, radiotherapy, and adjuvant cisplatin proportions	APaT population	ITT population	*CiC*	1.28	*CiC*

Abbreviations: 1L = first-line; APaT = all patients as treated; CiC = commercial in confidence; EF = event-free; EFS = event-free survival; ICER = incremental cost-effectiveness ratio; Incr = incremental; IRP = incurable recurrence/progression; ITT = intention to treat; L/SR = local or salvageable recurrence; OS = overall survival; Q3W = every three weeks; Q6W = every 6 weeks; QALY = quality adjusted life year; SoC = standard of care.

6.6 Key strengths

- The comparator was appropriate.
- The primary source of clinical data in the economic model was a phase III randomised study against the relevant comparator.
- The sources used to value costs in the model were appropriate.

6.7 Key uncertainties

- There was uncertainty in the set of distributions used to extrapolate transitions from the EF health state. While the survival analysis approach taken by the submitting company was reasonable, there were alternative extrapolations available that generated more pessimistic and optimistic EFS and OS benefits. These were considered in scenario analysis (Scenarios 1a and 1b, Table 6.3).
- There was uncertainty in the omission of an explicit cure assumption in the model. The submitting company viewed that when fitting parametric distributions to transitions from the EF state a clear plateau was already evident in the EFS hazards in the base case. To consider uncertainty related to this, scenario analysis explored an explicit cure assumption (Scenario 2).
- There were different censoring rules for EFS and OS outcomes in KEYNOTE-689. EFS was censored at the date of last disease assessment and OS was censored at the last date known alive. This created a minor internal consistency issue when considering transitions out of the EF health state in the multi-state modelling approach. If a patient had no progression event and no death event, then there was a choice whether to censor them at

the last assessment date (EFS rule) or at the last known alive (OS rule). In the base case, data for these patients were censored at the last assessment date in line with the EFS rule. This ensured that time spent in the EF state was only counted where progression-free status was observed, improving internal consistency and avoiding potential overestimation of time in the EF health state. This approach was viewed as the most appropriate. For completeness the submitting company provided a scenario that used the OS censoring rule instead for transition out of the EF health state (Scenario 3).

- An area of uncertainty was that the submitting company used the APaT population rather than the ITT population in the model to inform proportions undergoing initial surgery, radiotherapy, and adjuvant cisplatin from KEYNOTE-689. The submitting company viewed this as a more relevant population as it was based on patients who received least one dose of study intervention or surgery as part of KEYNOTE-689. It noted this was expected to better represent the resource use observed in clinical practice. Nonetheless, for completeness, a scenario was provided which considered the ITT population. The ICER impact was a modest increase (Scenario 11).

7 Conclusion

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

8 Guidelines and Protocols

The 'Head and Neck Cancer: United Kingdom National Multidisciplinary Guidelines' describe the treatment pathway for head and neck cancer in the UK.[5]

The European Head and Neck Society (EHNS), the European Society for Medical Oncology (ESMO) and the European Society for Radiotherapy & Oncology (ESTRO) [EHNS–ESMO–ESTRO] Clinical Practice Guideline provides key recommendations for managing squamous cell carcinoma of the oral cavity, larynx, oropharynx and hypopharynx.[4]

9 Additional Information

9.3 Product availability date

17 February 2026

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per course
pembrolizumab	**Neoadjuvant pembrolizumab: 2 doses of 200 mg every 3 weeks or 1 dose of 400 mg** **Adjuvant treatment with pembrolizumab: 3 doses of 200 mg every 3 weeks or 2 doses of 400 mg every 6 weeks**	**£89,420**

	Maintenance treatment with pembrolizumab: 12 doses of 200 mg every 3 weeks or 6 doses of 400 mg every 6 weeks	

Costs from BNF online on 01 June 2026. 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 300 patients eligible for treatment with pembrolizumab in year 1 rising to 318 patients in year 3.

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. This template does not incorporate any PAS discounts associated with comparator medicines or PAS associated with medicines used in a combination regimen.

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

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This assessment is based on data submitted by the applicant company up to and including 16 July 2026.

**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 includes Scottish national contract prices in its decision-making. These contract prices are commercial in confidence and cannot be put in the public domain, including via the SMC Detailed Advice Document.

Patient Access Schemes (PAS): A PAS 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. The Patient Access Scheme Assessment Group (PASAG), established under the auspices of Public Services Delivery Scotland, reviews and advises NHS Scotland on the feasibility and acceptability on implementing proposed schemes. PASAG operates separately from SMC to maintain the integrity and independence of the assessment process of the SMC. When SMC accepts a medicine for use in NHS Scotland on the basis of a PAS that has been considered acceptable for implementation by PASAG, a set of guidance notes on the operation of the scheme will be circulated to health boards' Area Drugs and Therapeutics Committees 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.