SMC2519

nivolumab 10mg/mL concentrate for solution for infusion (Opdivo®)

Bristol Myers Squibb

05 May 2023

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 assessed under the end of life and orphan equivalent medicine process

nivolumab (Opdivo®) is accepted for use within NHSScotland.

Indication Under Review: in combination with fluoropyrimidine- and platinum-based combination chemotherapy for the first-line treatment of adult patients with unresectable advanced, recurrent or metastatic oesophageal squamous cell carcinoma (OSCC) with tumour cell programmed death ligand 1 (PD-L1) expression ≥1%.

Addition of nivolumab to fluoropyrimidine- and platinum-based combination chemotherapy significantly increased overall and progression-free survival in patients receiving first-line treatment for advanced, recurrent or metastatic OSCC with PD-L1 expression ≥1%.

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

This advice takes account of the views from a Patient and Clinician Engagement (PACE) meeting.

Chair
Scottish Medicines Consortium

1. Clinical Context

1.1. Medicine background

Nivolumab is a monoclonal antibody that targets the programmed death-1 (PD-1) receptor and blocks interaction with its ligands, PD-L1 and PD-L2, leading to potentiation of T-cell responses including anti-tumour responses. It is administered intravenously at a dose of 240mg every 2 weeks or 480mg every 4 weeks until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression. [1]

1.2. Disease background

The incidence of oesophageal cancer increases with age and risk factors include smoking, alcohol consumption and poor socioeconomic status. It has two histologic types, squamous cell carcinoma and adenocarcinoma, with differing prognosis. At diagnosis, approximately 50% of oesophageal cancers are locally or loco-regionally advanced and thus amenable to potentially curative loco-regional therapy. Advanced, recurrent or metastatic oesophageal cancers are generally incurable and treated with palliative intent.[2]

1.3. Treatment pathway and relevant comparators

Patients with advanced or metastatic oesophageal cancer can receive localised treatments, such as radiotherapy or endoscopic therapies for symptomatic treatment of obstruction and dysphagia. For patients with good performance status, chemotherapy is the main palliative therapy and first-line treatment generally comprises a doublet regimen with a fluoropyrimidine (5-fluorouracil [5-FU] or capecitabine) plus platinum (cisplatin or oxaliplatin).[2 3] In May 2022, SMC issued advice (SMC2420) that the immunotherapy, pembrolizumab, is accepted for use with a restriction of a two-year stopping rule in the following indication: in combination with platinum and fluoropyrimidine based chemotherapy, for the first-line treatment of patients with locally advanced unresectable or metastatic carcinoma of the oesophagus in adults whose tumours express PD-L1 with a combined positive score (CPS) ≥10.

1.4. Category for decision-making process

Eligibility for a Patient and Clinician Engagement (PACE) meeting:
Nivolumab meets SMC end of life criteria and orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence was from the open-label phase III study, CheckMate 648, which compared nivolumab-chemotherapy versus chemotherapy and nivolumab-ipilimumab versus chemotherapy.[4] The latter comparison is not relevant to this submission and details of it are not presented.

Table 2.1. Overview of relevant studies

Criteria	CheckMate 648[2, 4]
Study Design	Open-label, international, phase III.
Eligible Patients	Adults (≥18 years) with unresectable advanced, recurrent or metastatic OSCC who had not received systemic therapy for advanced disease. Measurable disease on RECIST v 1.1 and ECOG performance status of 0 or 1.

Treatments	Nivolumab 240 mg IV every 2 weeks plus chemotherapy. Chemotherapy alone (28-day cycles of 5-FU 800 mg/m^2 IV daily on days 1 to 5 and cisplatin 80 mg/m^2 on day 1). Treatment continued until disease progression, unacceptable toxicity, withdrawal of consent or end of study. Nivolumab given for up to 2 years, maximum.
Randomisation	Randomisation was stratified by tumour cell PD-L1 status (≥1% versus <1% or indeterminate), region (East Asia [Japan, Korea, Taiwan] versus rest of Asia [China, Hong Kong, Singapore] versus rest of world), ECOG performance status (0 versus 1) and number of organs with metastases (≤1 versus ≥2). Patients were equally assigned across the treatment groups.
Primary outcomes	The co-primary outcomes were assessed in all randomised patients with tumours expressing PD-L1 ≥1% and were: Overall survival, defined as the time from randomisation to any cause death; and PFS, defined as the time from randomisation to progressive disease assessed by BICR using RECIST v 1.1 or death due to any cause.
Secondary outcomes	Overall survival and PFS in all randomised patients. ORR in patients with PD-L1 ≥1% and in all randomised patients.
Statistical analysis	The primary and secondary endpoints were tested using the Bonferroni-based graphical approach in a complex hierarchical testing strategy.

BICR = blinded independent central review; ECOG = Eastern Co-operative Oncology Group (ECOG). 5-FU = 5-fluorouracil; IV = intravenous; ORR = objective response rate, defined as complete or partial response on RECIST v 1.1 by BICR; OSCC = oesophageal squamous cell cancer; PD-L1 = programmed death ligand 1; PFS = progression free survival; RECIST v 1.1 = Response Evaluation Criteria in Solid Tumors version 1.1.

At the data cut-off (1 March 2021) for final analysis of progression-free survival (PFS), minimum follow-up for overall survival in patients with PD-L1 ≥ 1% was 12.9 months and median was 23.7 months (range 12.9 to 40.7 months). In the primary analyses, in patients with PD-L1 ≥ 1%, addition of nivolumab to chemotherapy significantly increased PFS (time from randomisation to disease progression assessed by blinded independent central review [BICR] on Response Evaluation Criteria in Solid Tumors [RECIST] version 1.1 or death from any cause) and overall survival (time from randomisation to death from any cause). Secondary analyses, in all randomised patients, indicated that the between group difference was significant for overall survival, but not for PFS. Therefore, the objective response rate (ORR), defined as complete or partial response on RECIST version 1.1 assessed by BICR, was not formally tested within the pre-specified hierarchy. Results for the licensed population, patients with PD-L1 ≥1%, are detailed in Table 2.2 along with results from updated analyses at cut-off 4 October 2021, where minimum follow-up was 20 months.[2, 4] The company also provided results from a subsequent data cut-off but these were considered confidential by the company so cannot be presented here.

Table 2.2: Results of CheckMate 648 study in Patients with PD-L1≥1%.[2, 4]

Data cut-off	**1 March 2021**		**4 October 2021**	
	Nivolumab + chemotherapy (N=158)	**Chemotherapy (N=157)**	**Nivolumab + chemotherapy (N=158)**	**Chemotherapy (N=157)**
Progression Free Survival by BICR on RECIST v 1.1				
Events	117	100	123	101
Median (months)	6.9	4.4	6.9	4.4
Hazard ratio	0.65 (98.5% CI: 0.46 to 0.92)*		0.66 (95% CI: 0.50 to 0.87)	
12-month PFS	25%	10%	25%	10%

Overall survival				
Deaths	98	121	118	130
Median (months)	15.4	9.1	15.0	9.1
Hazard ratio	0.54 (99.1% CI: 0.37 to 0.80)*		0.59 (95% CI: 0.46 to 0.76)	
KM 12-month OS	58%	37%	58%	37%
KM 18-month OS			45%	21%
Objective response rate by BICR on RECIST v 1.1				
ORR	84 (53%)	31 (20%)	84 (53%)	31 (20%)
Difference	33% (95% CI: 24% to 43%)		33% (95% CI: 24% to 43%)	
Median DOR, months	8.4	5.7	8.4	5.7
CR	26 (16%)	8 (5.1%)	26 (16%)	8 (5.1%)

* primary outcome, significant within hierarchical testing strategy; BICR = blinded independent central review; CI confidence interval; CR = complete response; DOR = duration of response; KM = Kaplan-Meier estimated; ORR = objective response rate, defined as complete or partial response; OS = overall survival; PD-L1 = programmed death ligand 1; PFS = progression-free survival; RECIST v 1.1 = Response Evaluation Criteria in Solid Tumours version 1.1.

2.2. Health-related quality of life outcomes

Health-Related Quality of Life (HRQoL) was assessed using the EuroQol EQ-5D-3L and Functional Assessment of Cancer Esophageal (FACT-E) questionnaires, which were completed at screening and during treatment. At the 1 March 2022 cut-off, there appeared to be no differences between the treatment groups during the study for EQ-5D-3L utility index and visual analogue score (VAS).[5] In all groups, there were mean increases in FACT-E scores through to week 49. However, these improvements from baseline were not considered clinically meaningful.[4]

2.3. Indirect evidence to support clinical and cost-effectiveness comparisons

In the submission, an indirect comparison of nivolumab-chemotherapy versus pembrolizumab-chemotherapy supported a scenario economic analysis. This is detailed in Table 2.3.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	Bayesian network meta-analysis (NMA).
Population	Adults undergoing first-line treatment of locally advanced, unresectable or metastatic oesophageal squamous* cell cancer with PD-L1 CPS ≥10.
Comparators	Pembrolizumab-chemotherapy.
Studies included	CheckMate 648[4] and Keynote 590.[6]
Outcomes	Overall survival and PFS.
Results	Nivolumab-chemotherapy versus pembrolizumab-chemotherapy: Constant HR: Overall survival HR 1.28 (95% CrI: 0.86 to 1.89); PFS HR 1.30 (95% CrI: 0.92 to 1.87). Varying HR (log-logistic): Overall survival HR 1.03 to 1.37; PFS HR 1.12 to 1.22.
Company conclusion	Nivolumab-chemotherapy and pembrolizumab-chemotherapy have similar overall survival and PFS.

* analysis also included patients with adenocarcinoma; Chemotherapy in both studies comprised 28-day cycles of 5-fluorouracil 800 mg/m^2 IV daily on days 1 to 5 and cisplatin 80 mg/m^2 on day 1; CPS = composite positive score; CrI = credible interval; HR = hazard ratio; PD-L1 = programmed death ligand 1; PFS = progression free survival.

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

3. Summary of Safety Evidence

In CheckMate 648, addition of nivolumab to chemotherapy increased toxicity, with higher rates of established adverse events. However, these were considered manageable. At the 1 March 2021 cut-off, median duration of treatment in the nivolumab-chemotherapy group was 5.7 months and in the chemotherapy group was 3.4 months. Adverse events were reported by almost all patients, 99% (308/310) and 99% (301/304) and were considered treatment-related in 96% and 90%, respectively. In the nivolumab-chemotherapy group, compared with chemotherapy, there were higher rates of serious adverse events, 58% versus 42%; treatment-related serious adverse events, 24% versus 16%; adverse events leading to discontinuation of study treatment, 41% versus 25%; and treatment-related adverse events leading to discontinuation of study treatment, 34% versus 19%, respectively.[2]

At the 1 March 2021 cut-off, in the nivolumab-chemotherapy and chemotherapy groups gastrointestinal adverse events were common, including nausea (59% and 52%), vomiting (18% and 16%), diarrhoea (19% and 15%), constipation (19% and 22%) and stomatitis (32% and 23%). Haematological adverse events were also frequently reported, such as anaemia (30% and 22%) and decreased counts of neutrophils (21% and 17%), white cells (14% and 9.2%) and platelets (12% and 11%). Other common adverse events included decreased appetite (43% and 43%), fatigue (20% and 16%), malaise (16% and 15%), hiccups (14% and 17%) and alopecia (10% and 11%).[2, 4]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- In CheckMate 648, addition of nivolumab to fluoropyrimidine- and platinum-based combination chemotherapy significantly increased overall survival and PFS in patients receiving first-line treatment for advanced, recurrent or metastatic OSCC with PD-L1 ≥ 1%. Although the analysis of overall survival was at an interim cut-off, it met the pre-specified criteria for significance at that point and the analysis was considered final. Effects on overall survival and PFS were considered clinically relevant in a regulatory review.[2]
- Nivolumab is one of two PD-L receptor inhibitor immunotherapies licensed in combination with platinum plus fluoropyrimidine chemotherapy for first-line treatment of locally advanced unresectable or metastatic OSCC. Nivolumab can be used in a wider population than the other immunotherapy, pembrolizumab, as it can be given to patients with PD-L1 ≥1% and is not limited to patients with PD-L1 CPS ≥10.[1, 7]

4.2. Key uncertainties

- There is no direct comparison of nivolumab-chemotherapy with the other immunotherapy-chemotherapy regimen licensed for use in this setting, pembrolizumab-chemotherapy. The indirect comparison of these regimens had some weakness, such as the inclusion of data from patients not eligible for treatment in practice: (a) a mixed population with OSCC and oesophageal adenocarcinoma provided PFS data for pembrolizumab-chemotherapy; and (b) patients with PD-L1 <1% were included in nivolumab-chemotherapy PFS and overall survival

analyses. Scenario 'overlap analyses', which compared data for nivolumab-chemotherapy patients with both PD-L1 ≥1% and PD-L1 CPS ≥10 versus pembrolizumab-chemotherapy patients with OSCC and PD-L1 CPS ≥10, produced results consistent with the primary analyses, but were limited by reduced sample size. There was omission of disease characteristics in the comparability assessment. A difference in median overall survival was noted in the chemotherapy control arms. The indirect comparison did not include safety and HRQoL outcomes. Despite these limitations, the company's conclusions seem reasonable.

- The open-label design of CheckMate 648 is unlikely to impact the co-primary outcomes, overall survival and BICR PFS. However, it may limit the assessment of subjective outcomes such as safety and quality of life. A regulatory review noted that no firm conclusions could be reached regarding quality of life outcomes due to the open-label design of the study and the exploratory nature of these endpoints.[2]
- In CheckMate 648, nivolumab was given in combination with 5-FU and cisplatin and there is no evidence for its use in this setting in combination with other fluoropyrimidine and platinum regimens. However, in practice nivolumab may be given in combination with other regimens such as capecitabine and oxaliplatin (CAPOX).
- The CheckMate 648 study did not permit inclusion of patients who had received prior checkpoint inhibitors, such as nivolumab. In May 2022, SMC issued advice (SMC2429) that nivolumab has been accepted for use as monotherapy for the adjuvant treatment of adult patients with resected oesophageal, or gastro-oesophageal junction cancer who have residual pathologic disease following prior neoadjuvant chemoradiotherapy. There are no data on the use of nivolumab for recurrent or metastatic disease in patients who have received it in the adjuvant setting.
- Approximately 70% of patients in CheckMate 648 were Asian. Within the primary analysis group (patients with PD-L1 ≥1%), pre-specified subgroup analysis by race were consistent with the primary analysis for overall survival (HR 0.57 and 0.48 in Asian and non-Asian patients) and PFS. Other pre-specified subgroup analysis of overall survival and PFS were generally consistent with the primary analyses.[2, 4, 5]
- In addition to the primary analysis population (PD-L1 ≥1%), CheckMate 648 included patients with PD-L1 <1% or indeterminate. However, nivolumab is not licensed in the latter subgroups. A regulatory review noted that its benefit in these patients is unclear and should be weighed against potential added toxicity.[2]

4.3. Clinical expert input

Clinical experts consulted by SMC considered that nivolumab fills an unmet need in this therapeutic area. Nivolumab is a therapeutic advancement due to improved overall survival compared with the current standard of care that comprises doublet chemotherapy. Additionally, it can be given to a wider group of patients compared with the other immunotherapy licensed for use in this setting. Clinical experts consulted by SMC note that there may be a service impact associated with development of testing to identify patients for treatment with nivolumab in this setting.

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

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

5. Patient and clinician engagement (PACE)

A patient and clinician engagement (PACE) meeting with patient group representatives and clinical specialists was held to consider the added value of nivolumab, as an orphan equivalent and end of life medicine, in the context of treatments currently available in NHSScotland.

The key points expressed by the group were:

- Advanced, recurrent or metastatic squamous oesophageal carcinoma is an incurable, life-limiting and severely debilitating condition. There are few available first-line treatments (typically fluoropyrimidine and platinum chemotherapy) and these have limited efficacy and substantial toxicity. There is an unmet need for well tolerated therapies that improve survival and quality of life.
- Addition of nivolumab to first-line standard care (fluoropyrimidine-platinum chemotherapy) improves progression-free and overall survival, with some patients reported to have exceptionally extended durations of survival, much greater than the average in the clinical studies. Patients may have an extended period when they are well, their disease is controlled and they can enjoy a good quality of life with their family. This may benefit their mental health and reduce their anxiety. Also, the knowledge that they have access to a new class of medicines may provide reassurance that they have optimum treatment for their condition and provide hope that the improved survival with nivolumab could be a bridge to a time when additional effective therapies become available.
- Availability of nivolumab would increase the immunotherapy treatment options available at this stage of the disease and provide an alternative for patients unable to receive the other immunotherapy. Also, it would increase the range of patients eligible for immunotherapy as it has a broader license than the other immunotherapy. Clinicians noted that it would not be an option for all patients and may be given only to those who are fit to receive combination therapy.
- Clinical experts noted that nivolumab is now an established treatment, with manageable toxicity, that can be given in peripheral units away from specialist centres. This may have benefits for patients who live in rural areas. Identification of patients for nivolumab requires testing for PD-L1, which may have service implications for pathology departments.

Additional Patient and Carer Involvement

We received patient group submissions from OCHRE, Guts UK Charity and Heartburn Cancer UK. All three organisations are registered charities. OCHRE has not received any pharmaceutical company funding in the past two years. Guts UK Charity has received 1.1% pharmaceutical company funding in the past two years, with none from the submitting company. Heartburn Cancer UK has received 5.95% pharmaceutical company funding in the past two years, including

from the submitting company. Representatives from all three organisations participated in the PACE meeting. The key points of their submissions have been included in the full PACE statement considered by SMC.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility
Time horizon	Lifetime (40 years)
Population	Adult patients with unresectable advanced, recurrent or metastatic OSCC with tumour cell PD-L1 expression ≥1%.
Comparators	The base case comparison was between nivolumab plus chemotherapy and chemotherapy alone. Within the base case chemotherapy was cisplatin plus fluorouracil. Alternative doublet chemotherapy regimens were considered in scenario analyses where acquisition costs were replaced and the alternative doublet regimens were assumed to have comparable effectiveness. A further scenario compared nivolumab plus chemotherapy against pembrolizumab plus chemotherapy. Pembrolizumab is only licenced in a PD-L1 CPS ≥10 population, therefore, the scenario only compares the two treatments within that CPS ≥10 group.
Model description	The analysis was based on a three-state partitioned survival model featuring the states of progression free, progressed disease and death.
Clinical data	The main source of clinical data was the CheckMate 648 study.[2, 4] An NMA was used to inform the comparison between nivolumab and pembrolizumab.
Extrapolation	A fully parametric approach was adopted where progression free survival and overall survival data from the CheckMate 648 were used to model patient outcomes using separately fitted parametric functions. Log-logistic distributions were applied for both arms for overall survival. Progression free survival was predicted using a lognormal distribution. Time on treatment was modelled according to observed Kaplan-Meier functions for both arms, with a maximum treatment duration for nivolumab of 24 months.
Quality of life	EQ-5D 3L data collected in CheckMate 648 were analysed to provide utility estimates by progression status. The CheckMate 648 whole population, including those with a PD-L1 <1%, was used as quality of life was not anticipated to vary by PD-L1 status, maximising data available for analysis. Utility values were estimated for the progression free and progressed disease states. Further utility decrements were applied as one-off adjustments for adverse events, and when patients entered their last 30 days before death.
Costs and resource use	First-line therapy and subsequent therapy medicine costs were included along with treatment management (administration and monitoring), and costs associated with adverse events. Subsequent therapy was assumed to be docetaxel or paclitaxel following nivolumab (or pembrolizumab) and nivolumab following doublet chemotherapy. The modelling included a cost of PD-L1 testing, valued at £42.61.
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 simple discount was offered on the list price. The results presented do not take account of the PAS for pembrolizumab, but this was 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.

6.2. Results

The base case economic results are presented in Table 6.2. Within that analysis chemotherapy was assumed to be cisplatin plus fluorouracil.

Table 6.2: Base case analysis (inclusive of PAS on nivolumab)

Technologies	ICER (£/QALY)
Chemotherapy	-
Nivolumab plus chemotherapy	31,363

QALY = quality adjusted life year; ICER = incremental cost-effectiveness ratio

The increase in costs for the nivolumab arm were primarily from the higher medicines acquisition costs. However, the use of nivolumab was also predicted to increase the time spent in the progression-free state, leading to an increased accumulation of quality adjusted life years.

6.3. Sensitivity analyses

The company provided sensitivity and scenario analysis exploring areas of uncertainty in the model. A selection of illustrative scenarios are presented in Table 6.3 below.

Table 6.3: Scenario analysis (inclusive of PAS on nivolumab)

#	Scenarios	Base case description	ICER (£/QALY)
1	Hybrid (updated data cut-off)	Fully parametric	47,039
2	Comparator: fluorouracil and oxaliplatin (FOLFOX)	Comparator: Chemotherapy (cisplatin plus fluorouracil	27,611
3	Comparator: capecitabine and oxaliplatin (XELOX)		29,090
4	Comparator: cisplatin plus capecitabine		31,908
5	Comparator: Pembrolizumab (PD-L1 CPS ≥10 population only)		Dominant*
6	No RDI applied to nivolumab	RDI applied to nivolumab	39,497
7	Removing time-to-death utility (30 days to death)	Time-to-death utility (30 days to death)	31,385
8	OS Weibull	OS log-logistic (both arms)	40,654
9	OS Generalized gamma		38,045

*KM=Kaplan Meire; RDI = Relative dose intensity; ICER = incremental cost-effectiveness ratio; QALY = quality adjusted life year. *nivolumab is estimated to be more effective with a lower cost. Note this result does not take account of the PAS for pembrolizumab, but this was considered in the results used for decision-making.*

6.4. Key strengths

- The analysis was based upon reasonably mature data from a directly relevant clinical study.
- Reasonable attempts were made to avoid over estimation of time on subsequent therapies.

6.5. Key uncertainties

- The choice of log-logistic distribution for overall survival was justified on goodness fit but alternative distributions with plausible extrapolations were reported to generate substantially lower mean overall survival. When overall survival estimates were extrapolated using the generalised gamma or Weibull distributions, the ICER increased (scenarios 8 and 9).
- Subsequent therapy after first-line treatment with chemotherapy was suggested by the submitting company to be nivolumab, and this is the basis on which costs accrue in the model. Use of nivolumab in CheckMate 648 appears to have been more limited, which may lead to post progression outcomes in the chemotherapy arm being under estimated relative to the assumed subsequent therapy costs.
- The indirect comparison between nivolumab and pembrolizumab showed only numerical differences between overall and progression free survival. Based on this a cost-minimisation analysis between the two treatments may have been more appropriate.

7. Conclusion

The Committee considered the benefits of nivolumab in the context of the SMC decision modifiers that can be applied when encountering high cost-effectiveness ratios and agreed that as nivolumab is an orphan equivalent medicine, SMC can accept greater uncertainty in the economic case.

After considering all the available evidence and the output from the PACE process, the Committee accepted nivolumab for use in NHSScotland.

8. Guidelines and Protocols

The National Institute for Health and Care Excellence (NICE) NICE guideline 83 (NG83) 'Oesophago-gastric cancer: assessment and management in adults' was published in January 2018.[3] See here

The European Society for Medical Oncology (ESMO) 'Oesophageal cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up' was published in July 2022.[8] See here

9. Additional Information

9.1. Product availability date

8 May 2022

9.2. Summary of product characteristics

See SPC for further information including dosing and safety. Nivolumab 10mg/mL concentrate for solution for infusion (Opdivo®) SPC

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per 4-week cycle (£)
Nivolumab	240mg every 2 weeks or 480mg every 4 weeks intravenously	**5,266**

Costs from BNF online on 8 December 2022. Costs calculated using the full cost of vials/ampoules assuming wastage. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

The company estimated there would be 66 patients eligible for treatment in year, to which confidential uptake rates were applied.

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.

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

References

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This assessment is based on data submitted by the applicant company up to and including 17 February 2023.

**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.