SMC2880

durvalumab concentrate for solution for infusion (Imfinzi®)

AstraZeneca UK Limited

05 June 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

durvalumab (Imfinzi®) is accepted for use within NHSScotland.

Indication under review: In combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by durvalumab as monotherapy adjuvant treatment after radical cystectomy, for the treatment of adults with resectable muscle invasive bladder cancer (MIBC).

Evidence from an open-label, phase III study demonstrated that the addition of perioperative durvalumab to neoadjuvant gemcitabine plus cisplatin significantly improved event-free survival and overall survival. Neoadjuvant gemcitabine plus 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

Durvalumab is a monoclonal antibody that inhibits the protein PD-L1, which is present on the surface of many cancer cells and prevents the immune system from attacking the cancer cells.[1] For muscle invasive bladder cancer, the recommended daily dose of durvalumab (in patients with a body weight greater than 30 kg) is 1,500 mg as an intravenous infusion in combination with chemotherapy every 3 weeks for four cycles prior to surgery, followed by 1,500 mg every 4 weeks as monotherapy for up to eight cycles after surgery. Patients with a body weight of 30 kg or less must receive weight-based dosing of durvalumab at 20 mg/kg. See the Summary of Product Characteristics (SPC) for more details.[2]

1.2. Disease background

Bladder cancer rates have fallen by 7% from 2013 to 2023 and is the eighth most common cancer in Scotland.[3] Muscle invasive bladder cancer means the cancer has spread into or through the muscle layer of the bladder, and accounts for approximately 25% to 30% of newly diagnosed bladder cancer cases.[4, 5] The most common presenting complaint is painless visible haematuria; other symptoms include non-visible haematuria, increased urinary urgency and frequency, dysuria, and in more advanced tumours pelvic pain and symptoms related to urinary tract obstruction.[6] The most important risk factor for developing bladder cancer is tobacco smoking, accounting for approximately 50% of cases.[7]

1.3. Treatment pathway and relevant comparators

The long-established standard of care treatment for patients with resectable muscle invasive bladder cancer is neoadjuvant cisplatin-based chemotherapy followed by radical cystectomy alone.[6, 7] In NHSScotland, the most common cisplatin-based regimen used is cisplatin plus gemcitabine. For a small number of patients with muscle invasive urothelial carcinoma (MIUC) with tumour cell PD-L1 expression ≥1%, who are at high risk of recurrence after undergoing radical resection of MIUC, nivolumab monotherapy is available as an adjuvant treatment option (SMC2503). The Cancer Medicines Outcomes Programme Public Health Scotland (CMOP-PHS) report for SMC confirmed that neoadjuvant gemcitabine plus cisplatin was the most relevant comparator and that a very small number of patients currently receive adjuvant nivolumab monotherapy in this setting.[8]

1.4. Category for decision-making process

Eligibility for a PACE meeting

Durvalumab meets SMC orphan equivalent criteria for this indication.

2. Summary of Clinical Evidence

2.1. Evidence for the licensed indication under review

Evidence to support the efficacy and safety of durvalumab for the treatment of resectable muscle invasive bladder cancer comes from the NIAGARA study. Details are summarised in Table 2.1.

Table 2.1. Overview of relevant studies[5, 9]

Criteria	NIAGARA
Study design	International, randomised, open-label, phase III study.
Eligible patients	• Aged 18 years or older • Histologically or cytologically documented muscle invasive bladder cancer • Clinical tumour stage of T2, T3, or T4a, N0 or N1, and M0 (according to the eighth edition of the AJCC Cancer Staging Manual) • Eligible for neoadjuvant cisplatin-based chemotherapy • Medically fit to undergo radical cystectomy • ECOG performance status of 0 or 1 • Have not received prior systemic chemotherapy or immunotherapy for treatment of MIBC • Creatinine clearance of at least 40 mL/minute per 1.73 m^2 of body-surface area
Treatments	• In the durvalumab group, patients received four cycles of neoadjuvant durvalumab (at a dose of 1,500 mg) with gemcitabine plus cisplatin (gemcitabine at a dose of 1,000 mg per m^2 of body-surface area and cisplatin at a dose of 70 mg per m^2 were given on day 1, and gemcitabine at a dose of 1,000 mg per m^2 was given on day 8) administered intravenously every 3 weeks, followed by radical cystectomy and then up to eight cycles of adjuvant durvalumab (at a dose of 1,500 mg) administered intravenously every 4 weeks, or • In the comparison group, patients received the same neoadjuvant regimen of gemcitabine plus cisplatin followed by radical cystectomy alone.
Randomisation	Patients were randomised equally. Randomisation was stratified according to clinical tumour stage (T2N0 or higher than T2N0), renal function (creatinine clearance of 40 to <60 mL per minute per 1.73 m^2 or ≥60 mL per minute per 1.73 m^2), and tumour PD-L1 expression level (high expression or low/no expression).
Primary outcome	The co-primary outcomes were: • pCR, defined as a pathological stage of T0N0M0 (assessed by BICR) • EFS, defined as the time from randomisation to progressive disease that precluded radical cystectomy, the first recurrence of disease after radical cystectomy, the expected date of surgery (in patients who did not undergo radical cystectomy), or death from any cause.
Key secondary outcomes	OS
Statistical analysis	A hierarchical statistical testing strategy was applied in the study with no formal testing of outcomes after the first non-significant outcome in the hierarchy. pCR was formally tested at one data-cut (January 2022); EFS and OS were controlled for type I error at both interim analysis and final analysis.

Abbreviations: AJCC = American Joint Committee on Cancer; BICR = blinded independent central review; ECOG = Eastern Cooperative Oncology Group; EFS = event-free survival; MIBC = muscle invasive bladder cancer; OS = overall survival; pCR = pathological complete response.

At interim analysis 2 (data-cut April 2024), perioperative durvalumab plus neoadjuvant gemcitabine plus cisplatin led to significant improvements in event-free survival; pCR was not significantly different between treatment groups. The multiplicity-controlled secondary outcome overall survival was also statistically significantly improved in the durvalumab treatment group.[9] See Table 2.2 for details.

Table 2.2. Key efficacy results for NIAGARA (data-cut: April 2024) (ITT population).[5, 9]

	Durvalumab plus neoadjuvant chemotherapy (n=533)	Neoadjuvant chemotherapy (n=530)
Co-primary outcome: event-free survival (as per BICR or central pathology review)		
Events, n	187	246
Median follow-up	34.7 months	27.7 months
Median EFS	NR	46.1 months
Hazard ratio (95% CI)	0.68 (0.56 to 0.82) p<0.001	
KM EFS rate at 24 months	68%	60%
Co-primary outcome: pathological complete response (data-cut January 2022)		
Patients with pCR	34%	26%
Odds ratio (95% CI)	1.49 (1.14 to 1.96) p=0.0038[a]	
Secondary outcome: overall survival		
Events, n	136	169
Median follow-up	42.3 months	39.6 months
Median OS	NR	NR
Hazard ratio (95% CI)	0.75 (0.59 to 0.93) p=0.0106	
KM OS rate at 24 months	82%	75%

[a] threshold for significance, p= 0.001

Abbreviations: BICR = blinded independent central review; CI = confidence interval; EFS = event-free survival; ITT = intention-to-treat; KM = Kaplan-Meier; NR = not reached; OS = overall survival; pCR = pathological complete response

2.2. Health-related quality of life outcomes

Health-Related Quality of Life (HRQoL) was assessed using the EORTC QLQ-C30 which was collected on day 1 of every cycle. In both treatment groups and for all scales a general trend towards deterioration from baseline was observed in the first 25 weeks, followed by a decrease in deterioration or a return to baseline levels thereafter. No differences between treatment groups were observed in the prioritised (Global Health Score/Quality of Life, physical functioning, fatigue, and pain) and non-prioritised EORTC QLQ-C30 scales.[5]

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

In the absence of direct evidence comparing perioperative durvalumab in combination with neoadjuvant chemotherapy with adjuvant nivolumab after surgery the submitting company presented an indirect treatment comparison. This has been used to inform an economic scenario analysis.

Table 2.3: Summary of indirect treatment comparison

Criteria	Overview
Design	The submitting company considered that standard ITC approaches were not appropriate due to differences in inclusion criteria, randomisation and control arms between the studies. Therefore, they used a survival-time adjusted ITC. This approach simulates a scenario in which patients in the NIAGARA control group who would be eligible for adjuvant nivolumab (that is, high risk patients with PD-L1 ≥1%) receive adjuvant nivolumab instead of no treatment.
Population	Adults with MIBC at high risk of recurrence after radical cystectomy and PD-L1 ≥1%.
Comparators	Nivolumab (adjuvant monotherapy).
Studies included	NIAGARA (for durvalumab) and CheckMate 274 (for nivolumab).[9, 10]

Outcomes	EFS and OS.
Results	The results suggest that durvalumab improved OS and EFS compared with the counterfactual control group (that is, eligible patients in the NIAGARA control group who were simulated to receive adjuvant nivolumab).

Abbreviations: CI = confidence interval; EFS = event-free survival; HR = hazard ratio; ITC = indirect treatment comparison; MIBC = muscle invasive bladder cancer; OS = overall survival; PD-L1 = programmed death-ligand 1

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

3. Summary of Safety Evidence

Evidence from NIAGARA supports the relative safety of the addition of perioperative durvalumab to neoadjuvant gemcitabine plus cisplatin. Neoadjuvant gemcitabine plus cisplatin is the most relevant comparator in this setting. Data below are presented from the April 2024 data-cut where median duration of follow-up was 42.3 months in the durvalumab plus neoadjuvant chemotherapy group and 39.6 months in the neoadjuvant chemotherapy group.[5]

In the durvalumab plus neoadjuvant chemotherapy and neoadjuvant chemotherapy groups respectively, 95% and 93% had any adverse event (AE) possibly related to any study treatment; 41% of patients in both groups had any grade 3 or 4 AE possibly related to any study treatment; 0.6% of both groups had any AE with outcome of death possibly related to any study treatment; 16% and 12% had any serious AE possibly related to any study treatment; 16% and 12% had any AE that led to discontinuation of any study treatment possibly related to any study treatment; 50% and 40% had any AE that led to dose delay or interruption of any study treatment.[5] The most common AEs with frequency of greater than 15% were constipation (39% versus 39%); diarrhoea (21% versus 14%); nausea (54% versus 48%); vomiting (19% versus 18%); asthenia (18% versus 18%); fatigue (36% versus 32%); pyrexia (21% versus 16%); anaemia (39% versus 40%); neutropenia (26% versus 31%); blood creatinine increased (18% versus 15%); neutrophil count decreased (15% versus 14%); decreased appetite (27% versus 25%); urinary tract infection (30% versus 29%); pruritus (15% versus 7.2%).[5]

Overall, no new safety concerns were identified for durvalumab in the NIAGARA study. The addition of perioperative durvalumab to neoadjuvant chemotherapy was associated with increased rates of serious AEs, treatment discontinuations, immune-mediated AE and serious post-surgery complications, however durvalumab did not impact the number of patients undergoing surgery. Regulators noted that there is a trend of increased toxicity with older age and highlighted the need for careful selection of patients who would benefit from treatment with perioperative durvalumab.[5] The SPC recommends monitoring for immune-mediated AEs and infusion-related reactions.[2]

4. Summary of Clinical Effectiveness Considerations

4.1. Key strengths

- Durvalumab in combination with neoadjuvant gemcitabine plus cisplatin is the first treatment to be licensed for the perioperative (neoadjuvant and adjuvant) treatment of resectable muscle invasive bladder cancer.

- NIAGARA is a phase III study that provides direct evidence with the most relevant comparator in Scottish clinical practice (neoadjuvant gemcitabine plus cisplatin).
- The addition of perioperative durvalumab to neoadjuvant gemcitabine plus cisplatin resulted in a 32% reduction in the risk of an EFS event (HR = 0.68 [95% CI: 0.56 to 0.82; p<0.001). EFS sensitivity analyses were overall consistent with the primary findings which confirms the robustness of the results. The benefit in EFS demonstrated can be considered clinically meaningful.[5]
- Overall survival was significantly improved in the durvalumab group compared with the control group. Median OS was not reached in either treatment group; HR = 0.75 (95% CI: 0.59 to 0.93; p=0.0106).[5]
- The addition of durvalumab to neoadjuvant gemcitabine and cisplatin did not lead to a reduction in proportion of patients who went for radical cystectomy, which is an important consideration in this curative setting.[5, 9]

4.2. Key uncertainties

- NIAGARA was an open-label study, which was in part mitigated by blinded independent central review of tumour assessments and blinding of the sponsor of the study. The lack of a placebo in the control group during the adjuvant phase may be a potential risk of bias.[5, 9] Due to the open-label design of the study, outcomes such as HRQoL and safety should be interpreted with caution.
- The benefit of durvalumab appears to be mainly driven by the subgroup of patients with greater than stage T2N0 disease (EFS HR = 0.61 [95% CI: 0.48 to 0.78]).[5] Patients with greater than stage T2N0 disease were likely overrepresented in the study since the number of patients with stage T2N0 disease was limited to a maximum of 40% of the total study population. Estimates of stage T2N0 disease in real-world settings are between 60 to 80%.[5, 11] This introduces some uncertainty in the generalisability of study results to the Scottish population.
- At data-cut April 2024 of NIAGARA, approximately 29% OS events had occurred which may be considered immature. Future OS analyses of NIAGARA will be descriptive only.[5]
- The ITC comparing perioperative durvalumab plus neoadjuvant chemotherapy with adjuvant nivolumab monotherapy had some limitations. The novel method of the ITC assumes the treatment effect of adjuvant nivolumab is exchangeable across the two included studies, however the study populations were notably different. For example, in CheckMate 274 about half of patients received neoadjuvant cisplatin chemotherapy whereas NIAGARA only recruited patients who were eligible for cisplatin-based chemotherapy.[9, 10] Despite this limitation, the results of the ITC appear reasonable. Adjuvant nivolumab monotherapy is a less relevant comparator in this submission.

4.3. Clinical expert input

Clinical experts consulted by SMC considered that durvalumab in combination with gemcitabine plus cisplatin fills an unmet need and is a therapeutic advancement for the treatment of resectable muscle invasive bladder cancer.

4.4. Service implications

The addition of perioperative durvalumab to neoadjuvant gemcitabine plus cisplatin may have some service implications for outpatient services.

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 Action Bladder Cancer, which is a registered charity.

- Action Bladder Cancer has received 5.2% pharmaceutical company funding in the past two years, with none from the submitting company.

- Bladder cancer patients with MIBC will have high grade tumours, these are difficult to treat and more likely to spread through the bladder wall and outside the bladder. MIBC is a disease with few treatment options and very poor patient outcomes and often little hope for patients or families.

- There is a substantial unmet need for new treatments for MIBC that demonstrate effectiveness in reducing recurrence and the current poor survival rate. Trial results for durvalumab demonstrate improved survival and progression free survival and that it reduces the risk of recurrence.

- In the current treatment pathway for MIBC patients the treatment plan at the point of diagnosis covers up to the point of major surgery, with decisions on further treatment decided after surgery. The availability of durvalumab would allow for a post-surgical treatment plan at the point of diagnosis, which is of substantial benefit to the patient.

6. Summary of Comparative Health Economic Evidence

6.1. Economic case

The submitting company provided an economic case as described in Table 6.1.

Table 6.1 Description of economic analysis

Criteria	Overview
Analysis type	Cost-utility analysis.
Time horizon	36 years (lifetime) with a starting age of 64
Population	In combination with gemcitabine plus cisplatin for the treatment of adults with muscle invasive bladder cancer (MIBC).
Comparators	Gemcitabine plus cisplatin
Model description	A partition survival model was used to demonstrate the cost-effectiveness of perioperative durvalumab. A four-state PSM including health states for event-free (EF), Locoregional recurrence (LR), distant metastases (DM) and death. The model had a 1-month cycle length which captured varying dosing schedules for the medicines included in the evaluation. A half-cycle correction was applied. The proportion of patients alive over time was estimated directly from the overall survival

	(OS) curve. Using the metastasis-free survival (MFS) curve, OS was then partitioned into the proportion of patients who are alive with distant metastases (DM) (OS minus MFS) and proportion of patients who are alive without DM (MFS). The event-free survival (EFS) curve further partitioned MFS into proportion of patients who were EF, based on the cumulative survival probabilities of EFS and those with a non-metastatic recurrence who occupied the LR state (MFS minus EFS). The LR state comprised of patients who failed or refused radical cystectomy (RC) surgery or experienced non-metastatic recurrence. Finally, the death state was estimated as one minus the cumulative survival probabilities for OS.
Clinical data	The main source of the clinical evidence for the economic evaluation was from the NIAGARA study[9], for the respective treatments, perioperative durvalumab vs. gemcitabine and cisplatin. The study was used to inform the baseline characteristics (age, body weight, body-surface area etc), treatment dosing and duration, survival (EFS, MFS and OS), adverse events (AEs), subsequent therapy proportions and surgery rates.
Extrapolation	Long-term extrapolation of OS, EFS and MFS was undertaken by the company for use in the economic model. Two different approaches of parametric survival analysis were conducted. Independent parametric survival analysis was used to extrapolate OS data. While more advanced/complex splines-based distributions were used for both MFS and EFS. Curve fit was based on a series of reported statistics which included hazard plot profiles, Schoenfeld residual plots, log-cumulative hazard plots and quantile-quantile (QQ) plots. Curve selection was based on goodness of fit statistics, visual fit and clinical expert opinion. These were further validated using external literature where available. The curves selected in the base case were: OS; perioperative durvalumab: Gompertz, gemcitabine and cisplatin: Log logistic EFS; perioperative durvalumab: Spline odds (1 knots), gemcitabine and cisplatin: Spline normal (2 knots) MFS; perioperative durvalumab: Spline hazard (1 knots), gemcitabine and cisplatin: Spline hazard (1 knots)
Quality of life	Health state utility values were based on an analysis of EQ-5D-5L utility data collected in the NIAGARA studies. EQ-5D-5L utility scores were mapped to EQ-5D-3L utility scores. Utility decrement from RC surgery was taken from the literature.[12] Disutility's associated with surgery were applied to the model to reflect the short-term reduction in HRQOL associated with surgery. Disutility's for AEs were included. Utilities were age adjusted in the model.
Costs and resource use	Costs included medicine acquisition costs, administration costs, subsequent treatment, management of AEs and surgery. Monitoring and resource use costs were also included in the model. Administration costs were included for the cost per IV administration. Treatment duration associated with perioperative durvalumab was also included in the model to reflect non perfect adherence to treatment protocols and used to calculate cost associated with perioperative durvalumab treatment. The data utilised was based on the observed proportions of patients who received each scheduled cycle in each arm of the NIAGARA study.[9]
PAS/contract price	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 NHS Scotland. Under the PAS, a discount of was offered on the list price.

Abbreviations: AE = adverse event; AIC = Akaike Information Criterion; BIC = Bayesian Information Criterion; DM = distant metastases; DR = distant recurrence; EF = event free; EFS = event-free survival; EQ-5D-3L = EuroQol 5-Dimension 3-Level questionnaire; EQ-5D-5L = EuroQol 5-Dimension 5-Level questionnaire; HRQoL = health-related quality of life; IV = intravenous; LR = locoregional recurrence; MFS = metastasis-free survival; MIBC = muscle-invasive bladder cancer; NHS = National Health Service; NIAGARA = NIAGARA clinical study; OS = overall survival; PAS = Patient Access Scheme; PASAG = Patient Access Scheme Assessment Group; PSM = partition survival model; QQ = quantile–quantile; RC = radical cystectomy.

6.2. Results

The base case results are presented in Table 6.2.

Table 6.2: Base Case Results (PAS prices)

Technologies	Total costs (£)	Total QALYs	Incr. LYG	Incr. costs (£)	Incr. QALYs	ICER (£/QALY)
Perioperative durvalumab + gemcitabine + cisplatin	CIC	CIC	CIC	CIC	CIC	14,872
gemcitabine + cisplatin	**CIC**	**CIC**	-	-	-	-

Abbreviations: ICER = incremental cost-effectiveness ratio; Incr. = incremental; LY = life year; QALYs = quality-adjusted life years

Most incremental costs in the perioperative durvalumab arm were attributed to treatment costs (durvalumab medicine, resource use and RC). In the perioperative durvalumab arm, most costs were incurred in the PF disease state (EFS), exceeding the progressive disease health state (LR and DM) costs. The same was the case for SoC arm. The majority of incremental QALY gains for perioperative durvalumab were generated in the progression free health state and secondly the progressive disease health state (mainly from distant recurrence disease). The majority of the incremental QALYs were gained after the initial trial period which meant that the benefit was mostly driven by modelled long-term extrapolation.

6.3. Sensitivity analyses

The company provided a range of sensitivity analyses. The deterministic one-way sensitivity analysis (OWSA) showed that the three parameters which had the greatest impact on the results were the percentage of patients undergoing RC in either treatment arm, the proportion of patients receiving subsequent treatment (in either treatment arm), the proportion of PD patients receiving carboplatin or avelumab in the comparator arm and EFS utility. Key scenario analyses are shown in Table 6.3

Table 6.3 Key scenario analyses

#	Parameter	Base case	Scenario	ICER (£/QALY)
Base case				14,871
1a	Time horizon (years)	36	20	16,451
1b			15	19,701
2a	EFS perioperative durvalumab	Flexible parameter survival models (Spline odds 1 knots)	Generalised gamma	15,726

2b	EFS gemcitabine and cisplatin	Flexible parameter survival models (Spline normal 2 knots)	Generalised gamma	15,428
3a	OS perioperative durvalumab	Gompertz distribution	Flexible parameter survival models	15,423
3b			log normal distribution	16,431
4a	OS gemcitabine and cisplatin	Log logistic	Flexible parameter survival models	18,956
4b			generalised gamma	18,296
4c			Gompertz	20,043
5	OS, MFS and EFS gemcitabine and cisplatin + OS, MFS and EFS - perioperative durvalumab	Various (See table 6.1)	best AIC distributions for all	24,717
6	Utility for DM health state	Based on NIAGARA study outcomes	Based on published literature (VESPER study): 0.62	15,217
7	Subsequent treatment proportions (SACT)	Based on treatment arm proportion in the NIAGARA study	Based on CMOP-PHS data – 24% for both treatment arms	16,270
8	Subsequent treatment proportions by category (SACT)	Based on clinical expert opinion	The same across both treatment arms (as gemcitabine and cisplatin)	16,422
9	Age at start of model	Based on NIAGARA study (64.4)	Based on CMOP-PHS data (66.5)	16,510
C1	Combined scenarios	Flexible parameter survival models (best AIC distribution) for OS (perioperative durvalumab and gemcitabine + cisplatin) **(3a + 4a)**		22,028

C2		Subsequent treatment proportions (SACT) + age at start of model based on CMOP-PHS + Best statistical fit/plausible alternative for OS **(20 + 22 + C1)**	25,222
C3		Age at start of model based on CMOP-PHS + Best statistical fit/plausible alternative for OS	22,162

Abbreviations: AIC = Akaike Information Criterion; C = combined CMOP-PHS = Cancer Medicines Outcomes Programme – Public Health Scotland; DM = distant metastasis; EFS = event-free survival; ICER = incremental cost-effectiveness ratio; MFS = metastasis-free survival; OS = overall survival; QALY = quality-adjusted life year; SACT = systemic anti-cancer therapy.

6.4. Key strengths

- The availability of randomised evidence that compared perioperative durvalumab to a relevant comparator in Scottish clinical practice that showed a statistically significant benefit in terms of EFS, MFS and OS for use in the economic model.
- The modelling approach utilised for the submission was appropriate given the disease condition and felt appropriate.
- Utility data were taken from the NIAGARA trial data.

6.5. Key uncertainties

- There was some uncertainty around the economic results as they relied on long-term extrapolation of NIAGARA study data over a 36-year horizon for EFS, MFS and OS. There was also uncertainty regarding the approach taken to select the curves to extrapolate the time to event outcomes for the base case analysis. This was most impactful for OS, where the company's base case curve selection utilised standard parametric models despite the observed KM data hazard profiles exhibiting similar characteristics as for EFS and MFS where the company utilised more flexible models instead. When the best fitting flexible models for all outcomes were used this resulted in a much higher ICER relative to the base case (Scenario C1).
- The hazard for death was constrained to values that are greater than or equal to the background all-cause mortality rate from the general population matched on age and gender, to avoid cases where survivorship in the cohort exceeds that of the general population. This meant that in the model those who had event-free MIBC in the durvalumab arm faced assumed the same mortality risk as the general population at later time points and this presented a face validity concern. A scenario that used a starting age that aligned with CMOP-PHS data resulted in an increased estimate of cost-effectiveness as it brought forward the required capping to general population mortality which is the point

at which the divergent OS curves across the treatment arms begin to converge (Scenario 9). Using the average age of patients with MIBC from the CMOP-PHS data was less impactful when applied to the best fitting flexible models to extrapolate OS were used, as these did not require capping to general population mortality to the same extent (Scenario C3).

- There was also some uncertainty regarding the proportions of patients receiving subsequent systemic anti-cancer therapy (SACT) in the economic analysis. Firstly, although proportions receiving subsequent treatment were informed by the multinational NIAGARA trial, there was a concern that this may not have been reflective of Scottish clinical practice as CMOP-PHS data indicated a lower proportion of patients receiving subsequent therapy. Secondly, additional uncertainty arose from the assumed mix of subsequent treatments, as base-case proportions were driven by expert opinion from a single clinician; when the distribution of subsequent treatments was assumed to be equal across the treatment arms, the ICER increased (Scenario 8). However, as the CMOP-PHS data were collected over an 18-month period, the proportion of patients who received a subsequent treatment observed in these data may underestimate the proportion who eventually receive a subsequent treatment over longer periods of time. Additionally, clinical experts consulted by SMC considered the proportion of patients and the distribution of subsequent treatments across the treatment arms of the model likely to be reflective of clinical practice in NHSScotland.

7. Conclusion

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

8. Guidelines and Protocols

The National Institute for Health and Care Excellence (NICE) published NICE Guideline 2 “Bladder cancer: diagnosis and management” in February 2015.[13]

The European Association of Urology (EAU) published guidelines on muscle invasive and metastatic bladder cancer in March 2026.[6]

The European Society for Medical Oncology (ESMO) published “Bladder cancer: ESMO clinical practice guideline for diagnosis, treatment and follow-up” in November 2021.[7]

9. Additional Information

9.1. Product availability date

12 August 2025

Table 9.1 List price of medicine under review

Medicine	Dose regimen	Cost per course (£)
durvalumab	**1,500 mg as an intravenous infusion in combination with chemotherapy every 3 weeks for four cycles prior to surgery, followed by 1,500 mg every 4 weeks as monotherapy for up to eight cycles after surgery**	**Up to £88,776 (12 cycles)**

Costs from BNF online on 03 April 2026. Costs do not take any patient access schemes into consideration.

10. Company Estimate of Eligible Population and Estimated Budget Impact

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.**

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13. National Institute for Health and Care Excellence (NICE). NICE guideline: Bladder cancer: diagnosis and management. Last reviewed September 2025. https://www.nice.org.uk/guidance/ng2 Accessed 08 April 2026.

This assessment is based on data submitted by the applicant company up to and including 22 April 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.