National Institute for Health and Care Excellence

Health Technology Evaluation

Durvalumab with gemcitabine and cisplatin before surgery (neoadjuvant) then alone after surgery (adjuvant) for treating muscle-invasive bladder cancer [ID6168]

Response to stakeholder organisation comments on the draft remit and draft scope

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Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	AstraZeneca UK	AZUK agree that it is appropriate to evaluate this technology through the single technology appraisal (STA) process	Thank you for your comment. No action needed.
	Action Bladder Cancer UK	This topic is highly appropriate for evaluation for a technology appraisal. Treatment options for muscle invasive bladder cancer are limited – there are significant unmet needs within this patient group. A large percentage of this patient group are not eligible for current treatment options due to other conditions or comorbidities, or treatment is not able to be continued or is unsuccessful. Patients often experience recurrence or spread of the disease. Other existing treatments can show high levels of lack of tolerability and adversely affect quality of life. It is of particular appropriateness given the trial results for Durvalumab which demonstrate improved survival, and progression free survival, versus the current most common treatment available for this patient group.	Thank you for your comment. No action needed.

Section	Stakeholder	Comments [sic]	Action
	British Uro-oncology Group (BUG)	Very appropriate. The trial results suggest a positive long term survival benefit for operable muscle invasive bladder cancer patients compared to standard treatment and is an important step forward in curing more people with MIBC.	Thank you for your comment. No action needed.
Wording	AstraZeneca UK	No comments	No action needed.
	Action Bladder Cancer UK	No comments	No action needed.
	British Uro-oncology Group (BUG)	Agree that wording of the remit reflects the issue(s) of clinical and cost effectiveness about this technology or technologies that NICE should consider.	No action needed.
Timing issues	AstraZeneca UK	Bladder cancer is the 9th most common cancer worldwide. Muscle-invasive bladder cancer (MIBC) patients, despite curative potential in some settings, face high-grade tumours which are harder to treat and more likely to spread to other tissues and organs, demanding immediate and aggressive intervention. There's an urgent need for treatments that have demonstrated efficacy in reducing the risk of relapse and disease-related mortality compared to the current standard of care.[1-8] According to experts consulted by AZUK, having an effective treatment for MIBC is extremely important as it represents the last chance for curing the patient. All efforts should be directed towards minimizing the risk of relapse as much as possible. With current treatments available, consulted experts believe that 1 in 2 patients will experience a relapse to metastatic urothelial cancer (mUC), demonstrating the urgency of having treatments that have proven to reduce the risk of relapse, especially those that have shown efficacy beyond	Thank you for your comment. No action needed.

Section	Stakeholder	Comments [sic]	Action
		the 2-year follow-up landmark, a point from which some clinicians define the cure of the patient.	
	Action Bladder Cancer UK	The availability of effective treatment options for this patient group facing poor outcomes is of pressing need, thus has an urgency for the NHS. There is also a need for rapid action to consider and assimilate new advances in treatment of bladder cancer into the health system. Due to the high recurrence rate, and likelihood of progression, together with continuing invasive monitoring, the lifetime treatment costs per patient of bladder cancer is the highest of all cancers.	Thank you for your comment. No action needed.
	British Uro-oncology Group (BUG)	This group of patients have poor outcomes. The treatment approach has been approved internationally and we would wish to offer UK patients the opportunity to benefit from the technology as soon as possible. This technology is not about extending life – more about increasing cure rates.	No action needed.
Additional comments on the draft remit	AstraZeneca UK	None	No action needed.
	Action Bladder Cancer UK	None	No action needed.
	British Uro-oncology Group (BUG)	None	No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	AstraZeneca UK	AZUK agrees with the data on epidemiology and available treatment options. However, further background information should be included on outcomes for patients with MIBC. This is imperative for stakeholders to understand the unmet need for this patient population and positioning of durvalumab in the treatment landscape and to conduct an accurate assessment of the technology. AZUK propose that the following paragraph is added into the background information section: "Despite radical cystectomy and cisplatin-based chemotherapy being available treatment options, MIBC patients remain at high risk of recurrence and progression to advanced cancer, with most recurrences occurring within 2 to 3 years after cystectomy. Disease progression is accompanied by a consequent deterioration in quality-of life, productivity, increased healthcare resource utilization (HCRU) and ultimately death as the five-year Overall Survival (OS) rate after treatment is less than 60%" [1-8]	Thank you for your comment. The comments have not been included as NICE aim to keep the background section of the scope brief. No action required.
	Action Bladder Cancer UK	NOTE: the following information is missing from the Background. Whilst more men than women are diagnosed with bladder cancer, women are more likely to be diagnosed at a later stage.	Thank you for your comment. The wording of the scope has been updated.
	British Uro-oncology Group (BUG)	Yes this reflects the current situation.	Thank you for your comment. No action needed.
Population	AstraZeneca UK	The population for the appraisal of this perioperative regimen should align with the expected license which is based on NIAGARA trial ([redacted]).[9]	Thank you for your comment. The population of the scope has been updated.

Section	Consultee/ Commentator	Comments [sic]	Action
	Action Bladder Cancer UK	The population is appropriate.	Thank you for your comment. No action needed.
	British Uro-oncology Group (BUG)	Yes, the population is appropriate.	Thank you for your comment. No action needed.
Subgroups	AstraZeneca UK	NIAGARA is the first Phase 3 perioperative immunotherapy study in MIBC and has demonstrated a statistically significant and clinically meaningful improvement in Event-free survival (EFS) and Overall Survival in the intent-to-treat (ITT) population, these outcomes support perioperative durvalumab with neoadjuvant chemotherapy (NAC) as the new standard treatment for patients with cisplatin-eligible MIBC.[4,10] To mitigate any potential imbalances across treatment arms concerning pivotal tumour characteristics that might prognosticate or influence treatment responsiveness, the randomisation process was stratified by disease stage, baseline PD-L1 expression, and renal function.[11] EFS and OS benefit were broadly consistent across all prespecified subgroups, therefore AZUK concludes no subgroups within the ITT population should be considered separately. As European Association of Urology (EAU) Guidelines on MIBC explain, PD-L1 expression in bladder tumours has been evaluated in several studies with mixed results, which may, in part, be related to the use of different antibodies and scoring methods. This variability, especially given the notable number of PD-L1-negative patients who still respond to immune checkpoint blockade, suggests that PD-L1 does not drive treatment decisions in MIBC or bladder cancer in general outside of patient selection for drugs that are restricted to a	Thank you for your comment. As you note, there is some uncertainty as to whether PD-L1 expression is prognostic effect. Given the uncertainty, the subgroups are kept inclusive at this stage to allow the committee the appropriateness of assessing subgroup results.

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		specific level of PD-L1 expression in the label. Leading specialists in the management of the disease, including urologists and oncologists, share the same view, as evidenced by the clinical guidelines of the EAU and European Society for Medical Oncology (ESMO).[3] It is in this context—and considering prior NICE recommendations such as technology appraisal guidance 817 for Nivolumab (TA817)—that AZUK understands the inclusion of PD-L1 as a subgroup of interest in the draft scope. TA817, based on the CheckMate-274 trial, reported hazard ratio (HR) values for the PD-L1 <1% subgroup for the primary endpoint of Disease-Free Survival (DFS) which were not statistically significant. The NIAGARA trial, the basis for this appraisal, demonstrated the subgroup analysis of the co-primary (EFS) and secondary (OS) endpoints according to PD-L1 expression levels as consistent with the ITT population. This indicates that PD-L1 is not influencing the efficacy of durvalumab with gemcitabine and cisplatin followed by durvalumab monotherapy in the NIAGARA trial.[9,12] AZUK suggests that the primary focus of this appraisal should remain the ITT population, as NIAGARA trial subgroup analysis does not suggest otherwise and the lack of evidence supporting PD-L1 as a treatment effect modifier for MIBC, in conjunction with the inherent limitations of subgroup analyses—which involve a lower number of patients and events—leaves PD-L1 expression non-informative for UK clinical practice in the context of this appraisal.	
	Action Bladder Cancer UK	Should be considered for all patients.	Thank you for your comment. No action needed.

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	British Uro-oncology Group (BUG)	The trial did not break down the impact of the technology according to PDL1 status. The value of PDL1 status and predicting benefit has been debated and has varied between studies. An attraction of treatment is that use may be independent status. Experience dictates that PDL1 status in some places takes weeks to return and waiting could add unhelpful and potentially detrimental delays to the patient pathway.	Thank you for your comment. As you note, there is some uncertainty as to whether PD-L1 expression is prognostic effect. Given the uncertainty, the subgroups are kept inclusive at this stage to allow the committee the appropriateness of assessing subgroup results.
Comparators	AstraZeneca UK	In MIBC clinical practice, only one decision point is required for the perioperative regimen evaluated in the NIAGARA trial (durvalumab with gemcitabine and cisplatin before surgery then durvalumab alone after surgery). No other perioperative regimen is available in clinical practice at the time of this appraisal. Therefore, appropriate comparators include cisplatin-based chemotherapy (i.e gemcitabine plus cisplatin) as neoadjuvant treatment followed by surgery. Comments on each comparator included in the draft scope are presented below: **As neoadjuvant (before surgery) treatment:** **Cisplatin-based chemotherapy** AZUK agrees that is the appropriate comparator for this appraisal. **Best supportive care** is not a relevant comparator for perioperative durvalumab as patients receiving this option would be eligible to receive	Thank you for your comment. Neoadjuvant best supportive care has been removed from the scope because as you note, the population in this appraisal is eligible to receive neoadjuvant cisplatin-based chemotherapy and therefore would not receive best supportive care. Adjuvant cisplatin-based chemotherapy has been removed from the scope because the

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		cisplatin-based therapy and would therefore be offered active therapy in clinical practice and not supportive care only. Cisplatin-based neoadjuvant chemotherapy is the standard first-line (1L) treatment in patients with MIBC fit enough to receive it. The combination of neoadjuvant therapy and radical cystectomy has shown potential for an increase in pathologic complete response (pCR), event-free survival (EFS), and overall survival (OS) in patients with MIBC.[3,14] According to NICE guidelines, neoadjuvant chemotherapy using a cisplatin combination regimen should be offered before radical cystectomy or radical radiotherapy to people with newly diagnosed MIBC for whom cisplatin-based chemotherapy is suitable.[13] **As adjuvant (after surgery) treatment:** AZUK has concluded that no adjuvant therapy constitutes an appropriate comparator for decision-making in this appraisal, due to the following reasons. The timing of the decision for a perioperative versus adjuvant approach differs. The decision for perioperative treatment is made prior to surgery, whereas the decision for adjuvant treatment is based on post-surgery outcomes. Therefore, these approaches are not directly comparable. This contrasts with comparisons of neoadjuvant and perioperative regimens, where the decision point for treatment is identical in both cases, reinforcing the relevance of neoadjuvant cisplatin as the appropriate comparator for this appraisal. Further details on each proposed comparator are listed below **Nivolumab as adjuvant treatment for people whose tumours express PD-L1 at a level of 1% or more** Nivolumab and durvalumab occupy distinct points in the treatment pathway and target different populations within MIBC. Therefore, they cannot be	majority of people would have received cisplatin-based chemotherapy as a neoadjuvant treatment and are not eligible for additional cisplatin as an adjuvant treatment. The comparators are kept inclusive at this stage to allow the committee to consider any comparator technologies for which evidence might be identified.

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		considered therapeutic alternatives and should not be compared to each other. Adjuvant nivolumab treatment, as outlined in TA817 and the CheckMate274 trial, is positioned for patients who, following radical cystectomy, are at high risk of recurrence (defined per tumour stage after surgery as any pT2-pT4a or pT0/x-pT4a/N+ for subjects who received neo-adjuvant cisplatin chemotherapy and any pT3-pT4a or pT0/x-pT4a/N+ subjects who have not received neo-adjuvant cisplatin chemotherapy and are not eligible for or refusing adjuvant cisplatin chemotherapy) and whose tumours express PD-L1 at a level of 1% or more, only if adjuvant treatment with platinum-based chemotherapy is unsuitable.[12] In contrast, perioperative treatment with durvalumab in combination with cisplatin-based chemotherapy must be administered before radical cystectomy, and patient selection is only based on eligibility for radical cystectomy and treatment with gemcitabine - cisplatin.[9-11] According to the current usage criteria based on the NICE decision on TA817, it is not possible to establish a potential treatment regimen that includes neoadjuvant chemotherapy, radical cystectomy followed by adjuvant nivolumab. This is because a treatment decision cannot be made at the point of neoadjuvant therapy since both the patient's risk of recurrence and PD-L1 status are unknown at that time. It is important to highlight that the use of adjuvant nivolumab has not demonstrated comparative evidence against the current standard of care - neoadjuvant cisplatin-based chemotherapy followed by surgery- in MIBC, as the comparator in the Checkmate-274 trial was placebo.	

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		The use of nivolumab as adjuvant therapy is, therefore, a reactive or salvage approach in response to a high risk of post-surgical recurrence. In contrast, any neoadjuvant or perioperative approach is a proactive strategy suitable for all eligible patients. To conclude, there is no overlap between both therapeutic approaches and therefore, nivolumab it is not a relevant comparator. **Cisplatin-based chemotherapy as adjuvant treatment** AZUKhas determined that adjuvant cisplatin should not be included as a relevant comparator for this appraisal, following a clinical consultation, for the following reasons: Adjuvant cisplatin is not the standard of care in the UK. As highlighted in TA817, the vast majority of cisplatin-eligible patients receive neoadjuvant cisplatin and are, therefore, not eligible for additional cisplatin. For patients who did not receive neoadjuvant therapy, there is limited evidence to support the use of adjuvant cisplatin-based ChT according to ESMO Guidelines and therefore, neoadjuvant ChT is preferred. As the NCRI-ACP-RCP-RCR joint response in TA817 highlighted, AZUK agrees that adjuvant cisplatin is the standard of care for the majority of patients who have not received neoadjuvant chemotherapy. [12,15] All candidates for the NIAGARA regimen will receive neoadjuvant chemotherapy and, consequently, will not be eligible for adjuvant cisplatin.[9-11] This demonstrates the lack of overlap between treatments and underscores that including adjuvant cisplatin as a comparator is not appropriate for decision making. **Best supportive care** is not a relevant comparator for perioperative durvalumab as patients receiving this option would be eligible to receive	

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		cisplatin-based therapy and would therefore be offered active therapy in clinical practice and not supportive care only. Therefore, it can be concluded that the only comparator of interest for this appraisal, based on the treatment decision point, patient population overlap, and comparative evidence, is cisplatin-based chemotherapy (i.e., gemcitabine and cisplatin) as neoadjuvant treatment followed by surgery.	
	Action Bladder Cancer UK	Consideration should be given whether the named comparators would be available for all patients in this MIBC group (eg: is a comparator only available for treatment for those with metastatic bladder cancer), and available through their NHS Trust.	Thank you for your comment. Accounting for geographical variances in treatment availability is beyond the remit of a NICE technology appraisal. Treatments for metastatic cancer are not relevant for this appraisal. No action needed.
	British Uro-oncology Group (BUG)	Best supportive care in the neoadjuvant is probably not correct terminology. The technology would only apply in people who would be suitable for neoadjuvant treatment as advised by NICE NG2 guidance. It is recognised that take up of neoadjuvant chemotherapy is suboptimal and underutilised. However we question whether the appraisal should be compared to (non recommended) cystectomy alone. It could be compared to cystectomy and adjuvant chemotherapy and or selected adjuvant immunotherapy – though as trial did not compare these comparators there is unlikely to be evidence to make such comparison.	Thank you for your comment. Neoadjuvant best supportive care has been removed from the scope because this population is eligible to receive neoadjuvant cisplatin-based chemotherapy. The comparators are kept

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			inclusive at this stage to allow the committee to consider any comparator technologies for which evidence might be identified.
Outcomes	AstraZeneca UK	Most of the outcomes included in the scope are aligned with those in the NIAGARA clinical trial. However, in the neoadjuvant and perioperative setting, **event-free survival (EFS), rather than progression-free survival (PFS), is the most appropriate endpoint because it accounts for progression events both before and after surgery**.[16,17] Surgery, combined with neoadjuvant and/or adjuvant therapy, is administered with the intent to cure, aiming to completely remove the primary tumour and minimise the risk of recurrence. Both progression that prevents surgery and recurrence after surgery are significant concerns for patients, due to their impact on subsequent prognosis and health-related Quality of Life (HRQoL). In the NIAGARA trial, EFS was defined as co-primary endpoint as the time from randomisation to the first recurrence of disease after radical cystectomy, the first documented progression in patients unable to undergo radical cystectomy, documented residual disease in patients who refuse radical cystectomy, or death from any cause, whichever comes first.[11] EFS, therefore, captures multiple significant events for patients, providing a direct assessment of treatment efficacy across neoadjuvant and adjuvant periods, and remains unaffected by treatments given after progression or recurrence. By including progression that precludes surgery, recurrence after surgery, and death, **EFS aligns with the therapeutic goals of this setting**	Thank you for your comment. The outcomes are kept inclusive at this stage therefore event-free survival and progression free-survival will remain as an outcome of interest. No action needed.

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		and evaluates the success or failure of neoadjuvant followed by adjuvant therapy.[16,17] **As EFS is positively correlated with OS, the statistically significant results for both EFS and OS in the NIAGARA trial suggest that a perioperative durvalumab regimen effectively delays progression to high-risk disease and metastasis**.[9,10] This is particularly important given that patients with muscle-invasive bladder cancer (MIBC) are at a high risk of disease recurrence and progression, conditions associated with poorer survival outcomes. NIAGARA is the first Phase 3 perioperative immunotherapy study in MIBC and has demonstrated a statistically significant and clinically meaningful improvement in EFS (HR, 0.68 (95% CI, 0.56–0.82), *P*<0.0001) and OS (HR, 0.75 (95% CI, 0.59–0.93), *P*=0.0106).[9] **Due to the limited utility of PFS for decision-making and its exclusion from the NIAGARA trial and other related studies in this appraisal, AZUK proposes that it be removed from the scope.**	
	Action Bladder Cancer UK	They are appropriate. However, it is key that the impact on patients being less likely to experience cancer recurrence, disease progression, not undergoing surgery, or death with durvalumab before and after surgery as compared with current treatment standard is given due weight.	Thank you for your comment. No action needed.

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	British Uro-oncology Group (BUG)	Yes	Thank you for your comment. No action needed.
Equality	AstraZeneca UK	AstraZeneca is not aware of any equality issues.	Thank you for your comment. No action needed.
	Action Bladder Cancer UK	See note re inequality of women being diagnosed at a later stage than men. Equality of access – would all patients be able to access new treatments – in particular rural areas, smaller hospitals etc.	Thank you for your comment. Treatment availability due to geographical location and timeliness of diagnosis is outside the remit of a NICE technology appraisal. No action needed.
	British Uro-oncology Group (BUG)	We don't forsee any equality problems. Having additional therapies such as these can be more challenging to apply to those that lack or have limited capacity. Rural patients may find accessing prolonged treatment more difficult.	Thank you for your comment. Treatment availability due to geographical location is outside the remit of a NICE technology appraisal. No action needed.
	AstraZeneca UK	No other comments.	No action needed.

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Other considerations	Action Bladder Cancer UK	There has a lack of new treatments available for bladder cancer – a common cancer with poor outcomes and high recurrence rates. It is important that this new treatment is viewed within that context. There is concern amongst patients, patient groups and clinicians about the slowness to approve new immunotherapies for use in treating bladder cancer in the UK, particularly in the context of paucity of other effective treatments available. There is an acute need for effective new treatments.	Thank you for your comment. No action needed.
	British Uro-oncology Group (BUG)	Though this treatment was tested in patients who had cystectomy. Up to 50% of UK patients have bladder preserving therapy (usually radiotherapy based) and we would be pleased if the committee if any decision (especially if positive) was extended to those who choose bladder preservation (which NG2 recommends should be offered to eligible patients. This includes consideration of the adjuvant phase of treatment in patients who change their mind from having cystectomy because they have had a major treatment response. It would be a retrograde step if the wish to have treatment that increases cures at same pushes people away for the QoL benefits of bladder sparing treatments. It is noted that initial results UK academic trial (RAD-IO) (presented on 14.2.25 at GU ASCO) using durvalumab has shown this can be combined with radiotherapy without any significant acute problems.	Thank you for your comment. NICE scopes and recommendations are evidence based, therefore NICE can only recommend a technology where evidence has been assessed for a specific population and have to be aligned with the anticipated marketing authorisation. No action needed.
Questions for consultation	AstraZeneca UK	Would durvalumab be given as both neoadjuvant and adjuvant treatment? Durvalumab will be given, [redacted]	Thank you for your comments. No action required.

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		[redacted] [redacted] Are there situations where durvalumab would be given either only as neoadjuvant or only as an adjuvant treatment? Durvalumab is to be administered as a perioperative regimen, meaning that when this treatment approach is chosen, the decision regarding patient's treatment would apply to both, neoadjuvant and adjuvant setting. However, according to the [redacted] Where do you consider durvalumab will fit into the existing care pathway for muscle-invasive bladder cancer? According to the benefits in event-free survival (EFS) and overall survival (OS) demonstrated in the NIAGARA clinical trial and corroborated by UK clinical experts, neoadjuvant durvalumab in combination with gemcitabine-cisplatin, followed by durvalumab monotherapy post-surgery, is likely to become the new standard of care for MIBC in the UK for patients who meet the following positioning criteria: They are candidates for radical cystectomy. They are eligible for gemcitabine-cisplatin chemotherapy. Eligibility criteria for gemcitabine-cisplatin will be defined according to medical expert opinion, considering factors such as a creatinine clearance of at least 40 ml per minute per 1.73 m^2 of body surface area, as included in the trial protocol.	

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		They have no contraindications for the use of durvalumab. Please select from the following, will durvalumab be: C. Prescribed in secondary care with routine follow-up in secondary care For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. The details regarding where each available treatment for resectable cisplatin-eligible MIBC is positioned in the UK clinical practice have been included in the section above, along with their appropriateness as comparators for the purpose of this appraisal. Would durvalumab be a candidate for managed access? Perioperative durvalumab combined with neoadjuvant chemotherapy led to significant improvements in event-free survival and overall survival compared to neoadjuvant chemotherapy, which is the current standard of care for MIBC patients in the UK. Therefore, due to the level of certainty of the benefit, and recognized practice-changing value of durvalumab in this indication, it is anticipated that routine commissioning should be achievable, and it would not be considered a likely candidate for managed access. Do you consider that the use of durvalumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? NIAGARA trial is a clinical practice changing study, and the first perioperative immunotherapy regimen to be approved in MIBC. The transformative value of	

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		this innovation impacts beyond the efficacy results and the benefits captured in the QALY calculation. AZUK would like to highlight those substantial health-related benefits, in particular those that impact patient lives, as they are the centre of the healthcare system. As mentioned by Fight Bladder Cancer UK in TA11233, although QALY calculations do consider several aspects of HRQoL, they often overlook patient-reported outcomes. These outcomes include the psychological advantages of accessing innovative treatments, a reduction in treatment-related burdens, and fewer hospital visits or interventions due to side effects.[18] In the particular case of NIAGARA regimen in MIBC, these outcomes include: Value of hope, conceived as patient risk-seeking preferences based on a potential substantial benefit.[19] This is particularly important for MIBC patients who undergo highly impactful surgery and neoadjuvant chemotherapy treatment with uncertain outcomes regarding the likelihood of achieving a cure or reducing the risk of recurrence. Knowing that the NIAGARA regimen has shown a reduction in the risk of recurrence in what represents the last opportunity for cure in bladder cancer enhances patients' and their families' ability to cope with difficult circumstances, promoting an emotional state that indirectly contributes to positive emotional outcomes and should also be considered. Option Value, commonly defined as the value of living longer to see future novel therapies, is a way patients and their loved ones perceive the impact of survival outcomes, which helps maintain hope, allowing them to better deal	

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		with the burden of the disease. This aspect is especially significant in therapeutic areas, such as bladder and advance or metastatic urothelial cancer, where promising novel agents are in development, aiming to change the treatment paradigm in the coming years.[19] Early treatment planning: a perioperative regimen such as NIAGARA is established right after diagnosis, allowing patients and caregivers the opportunity to plan approximately one year of their lives in advance, enabling them to make necessary adjustments to their daily lives beforehand. In addition to the clarity it provides about upcoming steps, this approach reduces the emotional impact of undergoing additional tests and receiving pessimistic news after having a radical surgery, which often happens when the need for adjuvant treatment arises in the current treatment pathway. This change in the patient journey will also be perceived as an improvement in the quality of care by healthcare professionals, an aspect that will be addressed further in the next section. Informal care and impact on caregivers and family members: It is estimated that approximately 18.64% of the total health cost of bladder cancer in the UK is due to informal care, the cost of unpaid care, that is, the time (work and/or leisure) that caregivers forgo, valued as provide unpaid care for relatives with cancer.[20] Utilizing innovative treatments that have proven to enhance the efficacy of the standard of care in MIBC, as this is the last stage where it is possible to prevent the disease from progressing to a metastatic stage, could alleviate some of this strain, enabling caregivers to resume their professional lives and societal contributions.	

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		Personal Social Services perspective: a regimen like NIAGARA, which has been shown to decrease the risk of recurrence and therefore avoid the impact of progressing to a metastatic stage, consequently improving the patient's quality of life and fostering autonomy, could result in reduced long-term care costs. By preserving higher levels of functionality and independence, effective treatments provide significant advantages both for the patient's well-being and in economic terms. The above-mentioned aspects not only positively impact the patient but also translate into improved quality of care from the perspective of the healthcare professional and the system. The reduction in the risk of relapse and progression to advanced stages of the disease, as well as the demonstrated overall survival, translates into potential cost savings for the system, as treatments associated with disease progression, along with hospital admissions, symptom management, and palliative care, are likely to decrease with fewer progressions. Early treatment planning has benefits from the perspective of both the healthcare professional and the system, as it allows for optimal scheduling of visits, clear and effective communication with the patient, and potentially prevents recurring visits to evaluate adjuvant treatment, if necessary, along with the associated tests (e.g., PD-L1). One of the added values for the system and healthcare professionals, which is difficult to capture in the QALY but has a significant impact, is the ability to	

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		address a recognised unmet need which carries even more weight in the case of MIBC, as it represents the last opportunity to cure the patient. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. The submission will be based on the NIAGARA clinical trial as evidence of the benefit of durvalumab in combination with gemcitabine-cisplatin, followed by durvalumab monotherapy post-surgery. Therefore, the benefits beyond the QALY will be derived from this evidence and the existing data to analyse the current bladder cancer landscape in the UK NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. No comments	
	Action Bladder Cancer UK	None	No action needed.
	British Uro-oncology Group (BUG)	Would durvalumab be given as both as both neoadjuvant and adjuvant treatment? Are there situations where durvalumab would be given either only as neoadjuvant or only as an adjuvant treatment? On the basis current data would suggest that in the vast majority of cases would be used as both neoadjuvant and adjuvant. It is unknown what the	Thank you for your comments. No action needed.

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		contribution of the adjuvant compared to neoadjuvant phase. It has been questioned whether adjuvant treatment is needed in people with pathological CR-but is uncertain. A completed trial-ImVigor 011may address this issue but no results are available and does noit directly reflect this situation However there may be the occasion where adjuvant treatment omitted if they had complications (eg significant autoimmune toxicity) when given neoadjuvantly. Some people have complications after cystectomy and may take extended time to recovery which may make adjuvant therapy difficult/inappropriate Where do you consider durvalumab will fit into the existing care pathway for muscle-invasive bladder cancer? Neoadjuvant cisplatin based chemotherapy is recommended by NG2 guidance to be offered to all patients with good PS, Adequate renal function, T2-3 urothelial cancer and no other cisplatin contraindications. We would expect that this technology will be considered for all cisplatin fit patients who are willing to consider surgery as their definitive treatment with no contraindications to immune therapy. Please select from the following, will durvalumab be: A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care C. Prescribed in secondary care with routine follow-up in secondary care D. Other (please give details): For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. No as per the study this treatment would be given exclusively in secondary care. Would durvalumab be a candidate for managed access?	

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		Uncertain as to the meaning of this context. It would be used at multiple sites but assume would be accessed using the usual High Cost drug applications via B* forms. Do you consider that the use of durvalumab can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Most likely No. Improved response rates and less cancer burdens may ensure that cystectomy is lower risk and have lower subsequent recurrence rates and require less adjuvant radiotherapy. Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits. Number of publications demonstrating high pelvic recurrence rates in patients with pT3 disease.	
Additional comments on the draft scope	AstraZeneca UK	References: 1. Torre LA, Siegel RL, Ward EM, Jemal A. Global Cancer Incidence and Mortality Rates and Trends--An Update. Cancer Epidemiol Biomarkers Prev. 2016 Jan;25(1):16-27. doi: 10.1158/1055-9965.EPI-15-0578. Epub 2015 Dec 14. PMID: 26667886. 2. Cancer Research UK 2022 3. Alfred Witjes J, Max Bruins H, Carrion A, Cathomas R, Comperat E, Efstathiou JA, et al. European Association of Urology Guidelines on Muscle-invasive and Metastatic Bladder Cancer: Summary of the 2023 Guidelines. Eur Urol. 2024;85(1):17-31.	Thank you for your comment. No action needed.

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		4. Alfred Witjes J, Lebret T, Compérat EM, Cowan NC, De Santis M, Bruins HM, Hernández V, Espinós EL, Dunn J, Rouanne M, Neuzillet Y, Veskimäe E, van der Heijden AG, Gakis G, Ribal MJ. Updated 2016 EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer. Eur Urol. 2017 Mar;71(3):462-475. doi: 10.1016/j.eururo.2016.06.020. 5. Koie T, Ohyama C, Imai A, Hatakeyama S, Yoneyama T, Hashimoto Y. Recurrence pattern after neoadjuvant chemotherapy compared to surgery alone in patients with muscle-invasive bladder cancer. American Society of Clinical Oncology; 2016. 6. Kaczmarek K, Malkiewicz B, Skonieczna-Zydecka K, Leminski A. Influence of Neoadjuvant Chemotherapy on Survival Outcomes of Radical Cystectomy in Pathologically Proven Positive and Negative Lymph Nodes. Cancers (Basel). 2023;15(19). 7. Esteban-Villarrubia J, Torres-Jimenez J, Bueno-Bravo C, Garcia-Mondaray R, Subiela JD, Gajate P. Current and Future Landscape of Perioperative Treatment for Muscle-Invasive Bladder Cancer. Cancers (Basel). 2023;15(3). 8. Moon S, Pandya V, McDonald A, Basu A, Bae S, Ferguson III JE, editors. Analysis of treatment of muscle invasive bladder cancer using the national cancer database: Factors associated with receipt of aggressive therapy. Urologic Oncology: Seminars and Original Investigations; 2023: Elsevier. 9. Powles T, Catto JW, Galsky MD, Al-Ahmadie H, Meeks JJ, Nishiyama H, et al. Perioperative durvalumab with neoadjuvant chemotherapy in operable bladder cancer. The New England journal of medicine. 2024:1-14 10. Powles T et al. Presented at: ESMO 2024 Congress. Abstract #LBA5	

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		11. AstraZeneca. Clinical Study Protocol: A Phase III, Randomized, Open-Label, Multi-Center, Global Study to Determine the Efficacy and Safety of Durvalumab in Combination with Gemcitabine+Cisplatin for Neoadjuvant Treatment Followed by Durvalumab Alone for Adjuvant Treatment in Patients with Muscle-Invasive Bladder Cancer (NIAGARA). 2021 12. Nivolumab for adjuvant treatment of invasive urothelial cancer at high risk of recurrence. (2022) NICE technology appraisal guidance 817. 13. Bladder cancer: diagnosis and management (2015) NICE guideline NG2. 14. Hamid A, Ridwan FR, Parikesit D, Widia F, Mochtar CA, Umbas R. Meta-analysis of neoadjuvant chemotherapy compared to radical cystectomy alone in improving overall survival of muscle-invasive bladder cancer patients. BMC Urol. 2020;20(1):158. 15. Powles, T. et al. Bladder cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up Annals of Oncology, Volume 33, Issue 3, 244 - 258 16. Ashish M. Kamat et al., Definitions, End Points, and Clinical Trial Designs for Bladder Cancer: Recommendations From the Society for Immunotherapy of Cancer and the International Bladder Cancer Group. JCO 41, 5437-5447(2023). DOI:10.1200/JCO.23.00307 17. Chavarriaga J. ESMO 2024: Evaluation of Event-Free Survival as a Surrogate Endpoint for Overall Survival in Muscle-Invasive Bladder Cancer Following Neoadjuvant Therapy. 2024. 18. Enfortumab vedotin with pembrolizumab for first-line treatment of unresectable or metastatic urothelial cancer who are eligible for platinum-containing chemotherapy [ID6332] In development [GID-TA11233] Expected publication date: 04 June 2025	

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		19. Tessa Peasgood, et al, Should We Consider Including a Value for "Hope" as an Additional Benefit Within Health Technology Assessment?, Value in Health, Volume 25, Issue 9, 2022,1619-1623, https://doi.org/10.1016/j.jval.2022.03.006. 20. Jose Leal, Ramon Luengo-Fernandez, Richard Sullivan, J. Alfred Witjes, Economic Burden of Bladder Cancer Across the European Union,European Urology, Volume 69, Issue 3,2016, Pages 438-447, https://doi.org/10.1016/j.eururo.2015.10.024.	
	Action Bladder Cancer UK	The draft Scope refers to Related NICE guidelines: Bladder cancer: diagnosis and management (2015) NICE guideline NG2. It is of some importance to note that this Guideline is now 10 years since publication in February 2015 (and reviewed evidence available to 2014). The Guideline does not adequately cover the introduction, evidence of efficacy and availability of new treatments for bladder cancer.	Thank you for your comment. No action needed.
	British Uro-oncology Group (BUG)	None	No action needed.

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

None