

NCPE Assessment

Summary

Durvalumab (Imfinzi®)

HTA ID: 25046

28 September 2026

Applicant: AstraZeneca

Durvalumab in combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by durvalumab as adjuvant monotherapy treatment after radical cystectomy, for the treatment of adults with resectable muscle invasive bladder cancer

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the cost-effectiveness of durvalumab (Imfinzi®) in combination with gemcitabine and cisplatin as neoadjuvant treatment, followed by durvalumab as adjuvant monotherapy treatment after radical cystectomy, in adults with resectable muscle invasive bladder cancer.

Following assessment of the Applicant's submission, the NCPE recommends that durvalumab (Imfinzi®) be considered for reimbursement, for this indication, if cost-effectiveness can be improved relative to existing treatments*.

The Health Service Executive (HSE) asked the NCPE to carry out an evaluation of the Applicant's (AstraZeneca) Health Technology Assessment of durvalumab (Imfinzi®). The NCPE uses a decision framework to systematically assess whether a technology is cost-effective. This includes comparative clinical effectiveness and health related quality of life benefits, which the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examines all the evidence which may be relevant for the decision; the final decision on reimbursement is made by the HSE. In the case of cancer drugs the NCPE recommendation is also considered by the National Cancer Control Programme (NCCP) Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

Summary

In March 2026, AstraZeneca submitted a dossier which investigated the comparative clinical effectiveness, cost-effectiveness and budget impact of durvalumab (Imfinzi®) in combination with gemcitabine and cisplatin (GemCis) as neoadjuvant treatment, followed by durvalumab as adjuvant monotherapy treatment after radical cystectomy (RC), in adults with resectable muscle invasive bladder cancer (MIBC). Throughout this report, durvalumab in combination with GemCis as neoadjuvant treatment, followed by durvalumab as adjuvant monotherapy after RC will be referred to as 'durvalumab + GemCis'. AstraZeneca is seeking reimbursement of durvalumab via the Oncology Drug Management System.

Durvalumab is a human monoclonal antibody that acts as a programmed death-ligand 1 (PD L1) inhibitor, by binding to PD-L1, preventing it from interacting with programmed-death 1 (PD-1) and CD80 (cluster of differentiation 80) receptors, enabling T-cells to destroy tumour cells. Durvalumab is administered by intravenous infusion. For the indication under assessment, durvalumab is given in combination with GemCis prior to RC at a recommended dose of 1,500mg once every three weeks for four cycles. Following RC, 1,500mg of durvalumab is administered once every four weeks for up to eight cycles as monotherapy. Treatment should continue until disease progression, unacceptable toxicity, or completion of the maximum number of cycles, whichever occurs first.

There are currently no perioperative therapies reimbursed for MIBC in Ireland. GemCis prior to RC is the current standard-of-care for patients with resectable MIBC undergoing RC who are eligible for platinum-containing chemotherapy. Throughout this report, this comparator is referred to as 'GemCis'. The Review Group agreed that neoadjuvant GemCis is a key comparator, but also considered adjuvant nivolumab relevant in this setting. Nivolumab is available following RC for patients at high risk of recurrence who have received platinum-based chemotherapy before RC. In response to request from the NCPE to include adjuvant nivolumab as a comparator, the Applicant provided an additional mixed treatment comparator including GemCis prior to RC for all patients with nivolumab after RC for a proportion of eligible patients. Throughout this report, this mixed treatment comparator is referred to as 'GemCis with adjuvant nivolumab'. The Applicant's proposed positioning of durvalumab is in line with the licensed indication.

1. Comparative effectiveness of durvalumab + GemCis

The main clinical evidence supporting the use of durvalumab + GemCis comes from the NIAGARA trial (n=1,063). NIAGARA is an ongoing, randomised, open-label, multicentre phase III trial examining the efficacy and safety of neoadjuvant durvalumab + GemCis followed by RC and adjuvant durvalumab monotherapy, as compared with neoadjuvant GemCis followed by RC alone in participants with MIBC. At inclusion, all patients had to be planning and medically fit to undergo a RC. Durvalumab was administered intravenously at a dose of 1,500mg once every three weeks for four cycles during the neoadjuvant phase and once every four weeks for up to eight cycles in the adjuvant phase. Neoadjuvant GemCis was administered every three weeks for the first four cycles as follows: gemcitabine at a dose of 1,000mg per body surface area (BSA)m² on Day One and Day Eight and cisplatin 70mg per BSA m² on Day One. The dual primary efficacy endpoints were event-free survival (EFS) assessed by blinded independent central review (BICR) and pathologic complete response (pCR) rates at time of cystectomy. Overall survival (OS) was a key secondary endpoint. Other secondary endpoints included metastatic-free survival (MFS), proportion of patients with RC, disease-free survival (DFS) and EFS assessed by investigator or local biopsy. Outcomes on health-related quality of life (HRQoL) were also collected. The most recent data cut was April 2024.

Median EFS per BICR was not reached in the durvalumab + GemCis arm, and was 46.1 months in the GemCis arm, with hazard ratio (HR) of 0.68 (95% confidence interval (CI) 0.56 to 0.82). The updated analysis of pCR rate demonstrated 37.3% in durvalumab + GemCis arm versus 27.5% in the GemCis arm, with odds ratio of 1.6 (95% CI 1.23 to 2.08). The median duration of follow-up for OS was 42.3 months for durvalumab + GemCis and 39.6 months for GemCis. Median OS was not reached in either arm, where 25.5% of participants died in durvalumab arm and 37.9% died in GemCis arm. HR for OS was 0.75 (95% CI 0.59 to 0.93). MFS and DFS results also favoured durvalumab. More patients underwent RC in the durvalumab + GemCis arm than in the GemCis arm (88.0% vs 83.2%), although the between-arm difference was not statistically significant. Pre-specified subgroup analysis of EFS showed that durvalumab was not associated with a statistically significant EFS benefit in participants with less advanced disease stage (T2N0) (HR 0.81; 95% CI 0.60 to 1.10). A post-

hoc subgroup analysis of OS indicated that durvalumab was not associated with a statistically significant OS benefit in participants with less advanced disease stage (T2N0) at inclusion.

The main limitations of the NIAGARA trial were an inability to isolate the relative contribution of neoadjuvant and adjuvant treatment phases on efficacy outcomes; the open-label nature of the study which may increase risk of bias, and an uncertainty whether the subsequent treatments in the trial are generalisable to clinical practice in Ireland.

Head-to-head trials were not available to provide direct comparative evidence for durvalumab + GemCis versus GemCis with adjuvant nivolumab. Indirect comparative methods are required to inform this comparison. The Applicant provided an indirect treatment comparison (ITC) of neoadjuvant GemCis versus a mixed treatment comparator GemCis with adjuvant nivolumab, based on generation of synthetic data for GemCis with adjuvant nivolumab. The ITC was used to inform the Applicant's cost-effectiveness model. The ITC used data from NIAGARA and Checkmate-274 trials.

2. Safety of durvalumab + GemCis

In the NIAGARA trial, adverse events (AEs) of grade 3 or 4 were reported in 69.4% participants in the durvalumab + GemCis arm and in 67.5% patients in the GemCis arm in the overall trial period (i.e. both the neoadjuvant + adjuvant periods). The majority of grade 3 or 4 AEs occurred in the neoadjuvant period. Grade 3 or 4 adverse drug reactions occurred in 41.9% and 43.5% of participants in the durvalumab + GemCis and GemCis arms, respectively. Serious adverse drug reactions occurred in 13.2% and 11.4% and resulted in death in 0.2% and 0.4% in the durvalumab + GemCis and GemCis arms respectively. The rate of discontinuation due to AEs was higher in the durvalumab + GemCis arm (21.1% versus 15.2%). However, among participants receiving neoadjuvant treatment, discontinuation rates were similar (14.9% versus 15.2%), noting that the control arm did not receive adjuvant therapy. The SPC states that the evidence on safety for patients aged ≥ 75 years was too limited to draw any conclusions for this population; this finding was consistent across multiple studies of durvalumab. The SPC also carries warning for specific immune-mediated events and infusion-related reactions.

3. Cost effectiveness of durvalumab + GemCis

The Applicant has compared the cost-effectiveness of perioperative durvalumab + GemCis with neoadjuvant GemCis. In addition, the Applicant also submitted a comparison with a mixed treatment comparator where a proportion of patients received adjuvant nivolumab in addition to neoadjuvant GemCis (GemCis with adjuvant nivolumab).

Methods

The cost-effectiveness model (CEM) was a partitioned survival model, with four mutually exclusive health states: event free (EF), local recurrence (LR), distant metastasis (DM) and death. The population was modelled based on the NIAGARA trial. All patients enter the model in the EF state and receive treatment with either durvalumab + GemCis in the intervention arm or GemCis alone in each comparator arm, followed by RC. After RC, patients in the intervention arm receive durvalumab monotherapy, patients in the GemCis arm receive no active treatment, and 13.8% of patients in the GemCis with adjuvant nivolumab arm receive nivolumab. Treatment effects for durvalumab and GemCis were informed by analysis of NIAGARA trial data. Relative treatment effects for nivolumab were based on Applicant's ITC using data from NIAGARA and Checkmate-274 trials. In each cycle, patients accrued quality adjusted life years (QALYs) and incurred costs based on the utilities (HRQoL values) and costs specified for the health-state occupied, the relevant treatment arm, and the time on treatment. Utilities for health states were informed by mixed model for repeated measures analysis of EQ-5D data from NIAGARA study. The CEM included drug acquisition costs, drug administration costs, subsequent treatment costs, disease management costs, AE costs and end-of-life costs.

The Review Group highlighted several uncertainties including: choice of model structure, assumption of cure and associated timepoint, representativeness and plausibility of utility values, and representativeness of subsequent treatments.

Results

Results of the Applicant base case deterministic cost-effectiveness analysis are presented in Table 1.

Table 1: Applicant base case incremental cost-effectiveness results^{a,b}

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
GemCis	98,086	6.44			
Durvalumab + GemCis	155,502	7.17	57,415	0.72	79,358
GemCis with adjuvant nivolumab	106,350	6.67			
Durvalumab + GemCis	155,502	7.17	49,152	0.50	98,973

GemCis: gemcitabine in combination with cisplatin; **ICER:** incremental cost-effectiveness ratio; **QALY:** quality adjusted life year

^a Corresponding probabilistic ICER using 1,000 iterations €79,767/QALY for GemCis and €97,921/QALY for GemCis+nivolumab. Figures in the table are rounded, and so calculations may not be directly replicable. Discount rate of 4% on costs and outcomes.

^b A commercial in confidence PAS is proposed for durvalumab and in place for nivolumab for the current indication, not included in this table.

The Review Group assessment identified a number of limitations in the Applicant's base case which were addressed in the NCPE adjusted base case. These included: increasing starting age in line with the population in Ireland, change of EFS extrapolation to generalised gamma, changing utilities for all health states due to capping EF utility value at general population utility, and change of treatment duration of nivolumab to reflect Checkmate-274 trial.

Table 2: NCPE adjusted base case incremental cost-effectiveness results^{a,b}

Treatments	Total costs (€)	Total QALYs	Incremental costs (€)	Incremental QALYs	ICER (€/QALY)
GemCis	99,208	5.99			
Durvalumab + GemCis	160,644	6.64	61,436	0.66	93,732
GemCis with adjuvant nivolumab	105,313	6.19			
Durvalumab + GemCis	160,644	6.64	55,530	0.45	121,697

GemCis: gemcitabine in combination with cisplatin; **ICER:** incremental cost-effectiveness ratio; **QALY:** quality adjusted life year

^a Corresponding probabilistic ICER using 1,000 iterations were €94,553/QALY for GemCis and €118,824/QALY for GemCis+nivolumab.

Figures in the table are rounded, and so calculations may not be directly replicable. Discount rate of 4% on costs and outcomes.

^b A commercial in confidence PAS is proposed for durvalumab and in place for nivolumab for the current indication, not included in this table.

Sensitivity analysis

Under NCPE adjusted base case assumptions, the probability of cost-effectiveness for durvalumab + GemCis at the €45,000/QALY threshold is 0% versus GemCis alone and 0.8% versus GemCis with adjuvant nivolumab. At the €20,000/QALY threshold, the probability is 0% for both comparators. A price-ICER analysis, using NCPE adjusted base case assumptions, indicated that price reductions of 60% and 65% (including the Framework Agreement rebate) would be required to meet the €45,000/QALY threshold, respectively. Price reductions of 83% and 86% would be required to meet the €20,000/QALY threshold, respectively.

4. Budget impact of durvalumab + GemCis

The price to wholesaler (PTW) of durvalumab is €2,390.98 per pack (1 x 500mg vial). Based on the mean number of administrations observed in the NIAGARA trial, the estimated cost per-patient, per-treatment course of durvalumab + GemCis is €72,630 (including VAT). Eligible patients comprise individuals with resectable MIBC who are undergoing RC and are candidates for cisplatin-based chemotherapy. The eligible patient numbers were estimated to be 52 in Year One, increasing to 55 in Year Five. However, both the eligible population estimates and the assumed market shares for durvalumab + GemCis are subject to uncertainty. The Applicant estimated a five-year cumulative gross drug budget impact of €9.8 million (including VAT) for durvalumab + GemCis. The corresponding five-year cumulative net drug budget impact was estimated to be €9.7 million (including VAT).

5. Patient Organisation Submission

No patient organisation submissions were received during the course of the assessment.

6. Conclusion

The NCPE recommends that durvalumab be considered for reimbursement if cost-effectiveness can be improved relative to existing treatments*.

*Next steps: The NCPE Assessment Report and recommendation will be considered by the HSE when making their decision on reimbursement, while also having regard to the criteria specified in the Health (Pricing and Supply of Medical Goods) Act 2013.

Further information on this process may be found [here](#).