Review of NICE, PBAC, and CDA HTA Outcomes For Oncology Drugs Approved by the FDA Through Project Orbis (2022-2023)

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Introduction

- Project Orbis is an FDA Oncology Center of Excellence led initiative that began in May 2019, designed to accelerate global access to innovative oncology treatments by coordinating regulatory reviews across 8 countries to reduce approval time and improve patient access[1].
- This research examined the reimbursement status of FDA-approved drugs under Project Orbis to explore how different HTA frameworks impact access to treatments in England, Australia, and Canada.

Methods

Drugs approved by the FDA through Project Orbis in 2022 and 2023 were identified (Project Orbis approvals document downloaded Dec 11, 2024)

→ NICE, PBAC, and CDA (previously CADTH) databases were searched (Dec 16, 2024) for HTAs of the corresponding drug approvals

→ Drugs with final guidance from all 3 HTA bodies were included for data extraction of pre-defined topics including recommendations, decision drivers, and inclusion of discounts and agreements

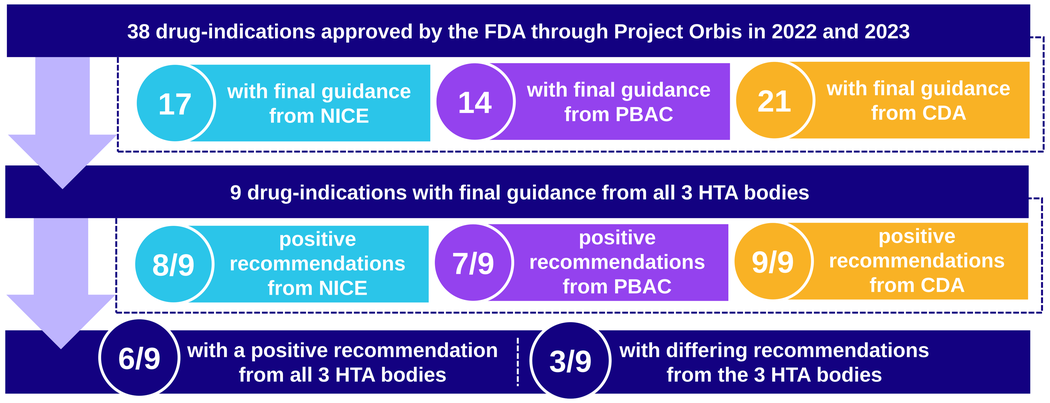
→ Final recommendations and key decision drivers for HTAs from NICE, PBAC, and CDA were compared

Results

NICE, PBAC, and CDA assessment of drugs approved by the FDA through Project Orbis

- Of the 38 drug-indications approved by the FDA through Project Orbis in 2022 and 2023, 9 received final guidance from all 3 HTA bodies (Figure 1).

Figure 1: *Search results for drugs approved by the FDA under Project Orbis in 2022 and 2023 and corresponding HTA from NICE, PBAC, and the CDA*



Drivers of positive recommendations from NICE, PBAC, and the CDA

- Positive recommendations (24/27 HTA; 89%) were driven by high unmet need, disease burden, improved clinical outcomes and acceptable CE.
- Severity modifiers were applied in 4/9 of the NICE assessments, of which 3 were recommended and 1 (trastuzumab deruxtecan in HER2-low breast cancer) was not.

Table 1: *Outcomes and committee critiques of clinical or economic uncertainty for HTA by NICE, PBAC, and the CDA*

Drug	Indication	NICE			PBAC		CDA	
		🔍	🪙	MAA	🔍	🪙	🔍	🪙
Belzutifan[a]	Von Hippel-Lindau disease	✓	✓	Y	×	✓	✓	✓
Dostarlimab	Primary advanced/recurrent endometrial cancer	✓	✓	Y	✓	✓	×	×
Darolutamide	Metastatic hormone-sensitive prostate cancer	×	✓	N	✓	✓	×	✓
Durvalumab	Advanced biliary tract cancer	✓	✓	N	✓	✓	✓	×
Elranatamab	Relapsed or refractory multiple myeloma	✓	✓	Y	✓	✓	✓	×
Nivolumab	NSCLC	✓	✓	N	✓	✓	✓	✓
Olaparib	High-risk early breast cancer	✓	×	N	✓	✓	✓	×
Trastuzumab deruxtecan	HER2-positive breast cancer	✓	✓	Y	✓	×	✓	✓
Trastuzumab deruxtecan	HER2-low breast cancer	×	×	-	✓	×	✓	×

Key: Recommended; Not recommended; 🔍 Critiqued for uncertainty in clinical trial data; 🪙 Critiqued for CE uncertainty

Note: [a]Drug first approved by the FDA through Project Orbis in 2021 in Von Hippel-Lindau disease requiring therapy for RCC, CNS tumors, or pancreatic tumors. It received subsequent FDA approval in RCC in 2023 (this indication has not been assessed by NICE, PBAC, CDA). As the Von Hippel-Lindau disease indication was included in the 2023 Project Orbis approvals database (downloaded Dec 11, 2024), it was included in this analysis.

Dependence of positive recommendations on agreements and discounts

- Uncertainty in clinical data or economic evaluations were common critiques across HTAs, most frequently critiqued by PBAC (9/9 HTA), followed by NICE (8/9) and CDA (8/9; Table 1).
- All positive recommendations either depended on agreements to allow for further data collection or discounts: all from NICE and CDA required price reductions, 86% (6/7) from PBAC required a RSA, and 50% (4/8) from NICE depended on a MAA (Table 1).
- NICE recommended 2 treatments (nivolumab in NSCLC, durvalumab in biliary tract cancer), despite clinical and economic uncertainty without a MAA, noting the limited treatments available and high unmet need.

Differing recommendations from NICE, PBAC, and the CDA

- There were 3 drug-indications with differing recommendations (Table 1).
- Negative recommendations were driven by lack of CE, limited generalizability to clinical practice, and data immaturity (Table 2).
- All HTA bodies consistently prioritized the applicability of comparators to clinical practice and alignment with treatment pathways.
- There were recommendations despite economic uncertainty, though these required price reductions (CDA), resubmissions to address concerns and RSAs (PBAC), or an ICER within the acceptable range (NICE).

Table 2: *Key decision drivers and committee considerations for HTA with differing recommendations from NICE, PBAC, and the CDA*

Drug	NICE	PBAC	CDA
Elranatamab	• Limited evidence on sustained efficacy but potential CE with longer-term evidence • Considered disease severity, and detriment to quality and length of life	• Trial not reflective of clinical practice in terms of SoC positioning • Magnitude of benefit unclear due to ITC limitations, impacting CE estimates	• Uncertainty in ITC, economic analysis, and budget impact
	✓ **Recommended** with MAA to mitigate uncertainty	✗ **Not recommended** Resubmission recommended to address committee comments	✓ **Recommended** with price reduction
Nivolumab	• Noted modelling uncertainties but ICER within acceptable range	• Uncertain CE estimates • Immature overall survival data	• Potentially cost-effective, despite modelling uncertainty
	✓ **Recommended**	✗ **Not recommended** Resubmission recommended to address committee concerns and Include RSA and price reduction	✓ **Recommended** with price reduction
Trastuzumab deruxtecan[a]	• Chemotherapy comparator from the trial was not fully generalizable to clinical practice SoC with a lack of reliable comparative evidence to appropriate comparator. • Lack of CE despite application of severity modifier	• This was an early re-submission to address prior critiques • Residual uncertainties in modeling remained • Demonstrated superiority vs. chemotherapy comparator	• Demonstrated superiority vs. chemotherapy comparator
	✗ **Not recommended**	✓ **Recommended** with RSA	✓ **Recommended** with price reduction

Note: [a]In HER2-low breast cancer.

Conclusions

- Project Orbis may accelerate regulatory approval, but does not guarantee access outside the US, with challenges in data uncertainty and demonstration of CE.
- While 89% of HTA were recommended, all depended on discounts or agreements to allow payers to accommodate an acceptable degree of uncertainty and avoid delays to patient access. Negative decisions were driven by lack of CE, limited generalizability to clinical practice, and data immaturity.
- The divergence in recommendations highlights the critical role of localized evidence. Critiques over choice of comparator and lack of evidence to support proposed treatment positioning underscores the need for clinical evidence that aligns with each country's treatment pathway and clinical practice.
- There is a need to plan early and optimize the evidence base, particularly for key model inputs, to mitigate uncertainty and payer risk, thereby avoiding the need for resubmission and increasing the likelihood of patient access.

Abbreviations: CADTH: Canadian Agency for Drugs and Technologies in Health; CDA: Canada Drug Agency; CE: cost-effectiveness; CNS: central nervous system; FDA: Food and Drug Administration; HER2: Human Epidermal Growth Factor Receptor 2; HTA: health technology assessment; ICER: incremental cost-effectiveness ratio; ITC: indirect treatment comparison; MAA: managed access agreement; NICE: National Institute for Health and Care Excellence; NSCLC: non-small cell lung cancer; PBAC: Pharmaceutical Benefits Advisory Committee; RCC: renal cell carcinoma; RSA: risk-sharing arrangement; SoC: standard of care; US: United States.

References: 1. FDA. Project Orbis 2025 [Available from: https://www.fda.gov/about-fda/oncology-center-excellence/project-orbis]; Included HTA by NICE, PBAC and CDA are detailed in publication supplement.

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