

TECENTRIQ & AVASTIN FOR HEPATOCELLULAR CARCINOMA - REIMBURSEMENT, COST OF THERAPY, AND DRUG PRICES IN CANADA

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Introduction:

The Canada's Provincial and territorial ministries of Health (does not include Quebec province) established Canadian Agency for Drugs and Technologies in Health (CADTH) pan Canadian Oncology Drug Review (pCODR) to search cancer drug therapies and make recommendations to guide the drug reimbursement decisions. The CADTH pCODR Expert Review Committee (pERC) takes decision on a Final Recommendation (Reimbursement).

It focuses mainly on two following points:

1. Clinical benefit
2. Economic evaluation

There are three categories of Reimbursement which pCODR categorizes the Reimbursement decisions,

1. Reimburse (Recommended)
2. Reimburse with clinical criteria and/or conditions (Conditionally Recommended)
3. Do not reimburse (Not Recommended)

Pricing and Cost of therapy for Tecentriq and Avastin in Canada

Atezolizumab (Tecentriq) costs US\$ 6,776.00 per 1,200 mg/20 mL.

Bevacizumab (Avastin) costs US\$ 519.178 per 100 mg/4 mL.

The recommended dose of 1,200 mg every three weeks for atezolizumab, the 21-day cycle costs US\$ 6,776.00 and the 28-day cycle costs US\$ 9,035.00. The recommended dose of 15 mg/kg every three weeks for bevacizumab, the 21-day cycle costs US\$ 5,711.00 and the 28-day cycle costs US\$ 7,615.00.

Atezolizumab is supplied as 1,200 mg vials for intravenous infusion. The recommended dosage regimen is 1,200 mg of atezolizumab in combination with 15 mg/kg of bevacizumab administered intravenously every three weeks until loss of clinical benefit or unacceptable toxicity. At the sponsor-submitted price of US\$ 6,776 per vial, the drug acquisition cost of atezolizumab is US\$ 6,776 per treatment cycle and US\$ 117,773 annually. In combination with bevacizumab, the total regimen cost is US\$ 11,021 per cycle and US\$ 191,555 annually.

pERC Recommendation Summary:

pERC conditionally (Reimburse with clinical criteria and/or conditions) recommends reimbursement of atezolizumab in combination with bevacizumab for first-line treatment of adult patients with unresectable or metastatic hepatocellular carcinoma (HCC) who require systemic therapy if the following condition is met:

- Cost-effectiveness improves to an acceptable level

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- Eligible patients should have no prior systemic treatment, have an Eastern Cooperative Oncology Group Performance Status (ECOG PS) of 0 or 1 and a Child-Pugh class status of A.
- pERC made this recommendation as it was satisfied that there is a net clinical benefit of atezolizumab plus bevacizumab compared with sorafenib based on a statistically significant and clinically meaningful improvement in overall survival (OS) and progression-free survival (PFS).
- pERC noted that atezolizumab plus bevacizumab is associated with significant but manageable toxicities.
- pERC acknowledged that there is no direct evidence that compares atezolizumab plus bevacizumab to lenvatinib for outcomes important to decision-making such as OS, PFS, and QoL. However, pERC noted that lenvatinib likely has efficacy similar to sorafenib (pERC based this on the REFLECT trial that demonstrated improved PFS, non-inferior OS and a different toxicity profile when comparing lenvatinib to sorafenib).
- The Committee concluded that, at the submitted price, atezolizumab plus bevacizumab is not considered cost-effective when compared with sorafenib or lenvatinib. pERC also noted the results of the cost-effectiveness analysis were driven by the high cost of both atezolizumab and bevacizumab; even with a substantial price reduction for each drug, it is highly unlikely atezolizumab plus bevacizumab would become cost-effective. pERC also concluded that the submitted budget impact analysis was underestimated and that the budget impact of atezolizumab plus bevacizumab at the submitted price would be substantial.
- It has been recommended on conditional basis that the Cost effectiveness of Drug should be acceptable and there should be no additional costs that patients should co-pay from their own pockets.

Pricing arrangements to improve cost-effectiveness: pERC was satisfied that there is a net clinical benefit with atezolizumab plus bevacizumab compared with sorafenib; therefore, jurisdictions may want to consider alternate pricing arrangements and/or cost structures to improve the cost-effectiveness to an acceptable level.

Pharmacoeconomic Report Submitted for Review:

Item	Description
Drug	Atezolizumab (Tecentriq), 60 mg / mL vial in combination with bevacizumab 100 mg or 400 mg vials for intravenous infusion.
Submitted price	Atezolizumab, 1200 mg / 20 mL, intravenous infusion: US\$ 6,776.00 per vial
Indication	Atezolizumab in combination with bevacizumab for the first-line treatment of adult patients with unresectable or metastatic hepatocellular carcinoma (HCC) who require systemic therapy.
Reimbursement request	Atezolizumab in combination with bevacizumab, for the treatment of patients with unresectable hepatocellular carcinoma (HCC) who have not received prior systemic therapy. Maintenance on either atezolizumab or bevacizumab should continue until loss of clinical benefit or unacceptable toxicity.
Sponsor	Hoffmann-La Roche Limited
Submitted results for base case (and key scenario analyses as	The sequential ICER for atezolizumab with bevacizumab was: <ul style="list-style-type: none"> • Atezolizumab plus bevacizumab Vs lenvatinib: US\$ 328,622 per

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required)	QALY (2.07 incremental QALYs, US\$ 332,281 incremental costs).
CADTH reanalysis results	<ul style="list-style-type: none"> Based on CADTH reanalyses, the sequential ICER (Incremental Cost Effectiveness Ratio) for atezolizumab plus bevacizumab versus sorafenib is US\$ 771,970 per QALY At a price reduction of 99% for atezolizumab, the ICER for atezolizumab plus bevacizumab is US\$ 309,306 per QALY gained. It is highly unlikely that atezolizumab plus bevacizumab would be considered cost-effective at a conventionally accepted ICER threshold (US\$ 50,000), unless there were significant price reductions for both atezolizumab and bevacizumab.

Conclusions:

CADTH undertook reanalyses of the sponsor’s economic submission to address above of the identified limitations.. Based on CADTH reanalyses, the sequential ICER for atezolizumab plus bevacizumab compared to lenvatinib was US\$ 771,970 per QALY gained. The results are primarily driven by the combined cost of treatment for atezolizumab plus bevacizumab. With a 99% price reduction for atezolizumab, the ICER decreases to US\$ 309,306 per QALY, exceeding US\$ 50,000 per QALY, as the cost of bevacizumab remains high.

Overall, it is highly unlikely that atezolizumab plus bevacizumab would be considered a cost-effective use of Canadian healthcare resources, at a US\$ 50,000 per QALY threshold, even if substantial price reductions were obtained for both atezolizumab and bevacizumab.

Sources: CADTH, PCODR, NY Times, Press Releases, Coherent Market Insights

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