The Budget Impact and Time Savings of Introducing Subcutaneously-Administered Nivolumab and Hyaluronidase (NIVO+Hyal SC) to Patients Receiving Intravenously-Administered Nivolumab (NIVO IV) Across Indications in Canada

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Background

- Nivolumab (NIVO) is a programmed cell death protein 1 (PD-1) inhibitor.[1]
- While NIVO is currently administered as a 30-minute intravenous (IV) infusion at dosing levels and frequencies that vary across indications[2], fixed-dose subcutaneous (SC) NIVO in combination with hyaluronidase (NIVO+Hyal) represents an alternative mode of administration and has the potential to improve the administration burden, tolerability, and patient and provider convenience.
- In May 2025, Health Canada approved NIVO+Hyal SC in 17 solid tumour indications.
- Approval was granted based on the results of the phase III trial - CheckMate 67T, comparing NIVO+Hyal SC to NIVO IV, which met pharmacokinetic non-inferiority endpoints.
- Currently, the Canadian healthcare system is facing increasing strain due to limited resources to manage the growing burden of cancer care[3].
- Given the large volume of NIVO patients, any opportunity to increase efficiencies would have an important effect in alleviating healthcare resource utilization (HCRU) strain in the Canadian healthcare system.
- To help inform various stakeholders, including but not limited to patients, healthcare practitioners (HCP) & payers, on the effect of integrating NIVO+Hyal SC into the Canadian healthcare system, a budget impact analysis (BIA) was developed.

Methods

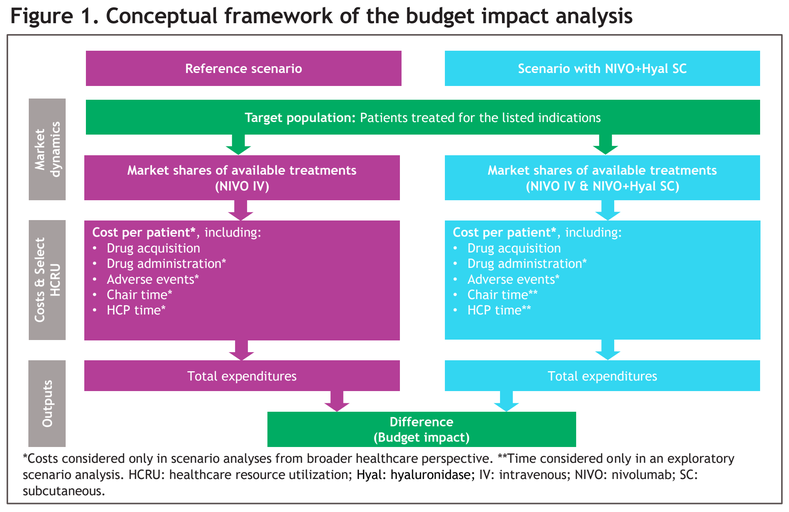
Objective

- To develop a BIA to quantify the economic impact, and the effect on select HCRU, of reimbursing NIVO+Hyal SC from a Canadian drug plan perspective, including from national & provincial levels.

Model structure

- The BIA assessed the impact of switching NIVO IV patients to NIVO+Hyal SC over 3 years across Canada.
- The BIA included drug acquisition costs, as well as exploratory analyses on chair time differences and healthcare practitioner (HCP) time savings related to drug preparation, administration, and monitoring.
- A top-down incidence-based epidemiology approach was used in this analysis.
- The BIA compares the following two scenarios (**Figure 1**):
  - A "reference scenario", where NIVO+Hyal SC is not available
  - A "scenario with NIVO+Hyal SC", where NIVO+Hyal SC is available

Figure 1. Conceptual framework of the budget impact analysis



*Costs considered only in scenario analyses from broader healthcare perspective. **Time considered only in an exploratory scenario analysis. HCRU: healthcare resource utilization; Hyal: hyaluronidase; IV: intravenous; NIVO: nivolumab; SC: subcutaneous.

Model parameters

- Model parameters (**Table 1**) were obtained from various sources: CheckMate trial (67T and indication-specific), BMS' internal data, and published literature.
- Epidemiology and HCRU inputs were sourced from published literature.

Perspective

- The base case analysis was from the public drug plan perspective in Canada at the national and provincial levels.
- Broader perspectives including select HCRU were considered in sensitivity analyses.

Discounting

- As per INESSS and CDA guidelines, and international best practices guidance, no discounting was applied in the BIA.[4,5]

Time horizon

- Budget impact was modeled over a 3-year horizon, using 2025 as the baseline year and with 2026, 2027, and 2028 designated as years 1, 2, and 3, respectively.

Patient clinical characteristics

- The target population aligned with the Health Canada-approved NIVO+Hyal SC indications which are also funded with NIVO IV.
- Mean weight was informed by INESSS', Quebec's health technology assessment agency, June 2025 submission guide, which in Appendix IV recommends to use an average weight of 76 kg & body surface area (BSA) of 1.85 m^2.[5]

Patient population

- Eligible patient population size was determined using:
  - Population of Canada[6]
  - Annual incidence rate of cancer in Canada[7] and published literature for specific tumor type
  - Proportion of patients receiving NIVO IV per indication[8,9]

Market shares

- In the "reference scenario", the share of NIVO+Hyal SC was set to 0% for all three years as it is not reimbursed, thereby limiting patients to NIVO IV as the only available option (100% over 3 years).
- In the "scenario with NIVO+Hyal SC", the average NIVO+Hyal SC market share uptake across indications was 12%, 24%, and 36% in years 1, 2, and 3, respectively. It should be noted that NIVO+Hyal SC uptake differed by indication, with slightly higher uptake in monotherapy indications & slightly lower uptake in indications with concurrent chemotherapy.

Treatment duration

- Treatment duration varied by indication and was according to NIVO-specific published literature but remained consistent between NIVO IV & NIVO+Hyal SC.[10]
- To determine appropriate treatment costs, the treatment duration was used to calculate number of doses received.

Cost inputs

- All cost inputs are presented in 2024 Canadian dollars (CAD).
- For all indications, an average body weight of 76.0 kg was applied as per INESSS guidance.[5]

Drug acquisition costs

- The cost per 600 mg single-dose vial of NIVO+Hyal SC was $4,107.00.
- The cost per 100 mg vial of NIVO IV was $1,955.56 and per 40 mg vial of NIVO IV was $782.22.[11]

Dosing and Cost

- The dosing schedules of NIVO IV and NIVO+Hyal SC were based on their respective Health Canada-approved product monographs.[10] In the base case analysis, the NIVO IV flat dose was used since the flat dose is available across all relevant indications whereas the weight-based dose is not, however, a weight-based NIVO IV dose approach across all indications was explored in a sensitivity scenario, which also allowed vial sharing.
- NIVO IV is available in Q2W, Q3W & Q4W dosing schedules, with a 240 mg, 360 mg & 480 mg, flat dose respectively, depending on the indication (see product monograph for available dosing schedule by indication). In the weight-based dosing scenario this corresponds to 3.0 mg/kg, 4.5 mg/kg & 6.0 mg/kg, respectively.
- NIVO+Hyal SC is only available as a fixed dose at Q2W, Q3W & Q4W schedules corresponding to 600 mg, 900 mg & 1200 mg, respectively.
- The cost per Q2W cycle per patient was $4,107.00 for NIVO SC, $4,693.32 for NIVO IV flat dose & $4,458.65 for NIVO IV weight-based dose (full vial sharing, 76 kg patient weight).

Administration costs

- Physician-related administration costs for inpatient costs were sourced from OHIP Schedule of Benefits and assumed to be applicable across Canada, except Quebec for which they were sourced from RAMQ Manuel des médecins spécialistes.[12,13]

Chair time & HCP time in scenario analysis

- The BIA captured healthcare resource use beyond drug costs, including staff (physician, nurse, pharmacist, pharmacy technician) time across pre-administration, administration, and monitoring
  - NIVO IV: ~30 min administration vs. NIVO+Hyal SC: 3–5 mins (4 mins in model, CheckMate 67T).[1]
  - Staff time inputs were sourced from the literature for oncologists and nurses time[14], as well as pharmacists and pharmacy technicians' time.[15]
  - SC staff time was estimated using percent reduction in treatment experience time from Waks et al. (2024).[16]

Adverse events

- The model considers injection-site related AEs, rash and pruritus, as user options for costs.[17] In the base case, they were not considered as there was found to be no significant difference in toxicity between the IV and Hyal SC formulations of NIVO in the pivotal CheckMate 67T trial.

Table 1. Summary of budget impact model scope

Component	Description
Perspective	Base case: Public drug plan perspective
Population	Adult patients with: • Unresectable or metastatic melanoma (monotherapy) • Unresectable or metastatic melanoma (combination) • Resectable melanoma as an adjuvant therapy • Metastatic NSCLC after progression on chemotherapy • Resectable NSCLC in the neoadjuvant setting • Recurrent or metastatic squamous cell carcinoma of the head and neck (SCCHN) after chemotherapy • Advanced renal cell carcinoma (RCC) • Intermediate- or poor-risk advanced RCC • Advanced RCC post-TKI treatment • High-risk urothelial carcinoma (UC) as an adjuvant therapy • Esophageal or gastroesophageal junction cancer (GEJC) as an adjuvant therapy • Advanced or metastatic gastric cancer (GC), GEJC, esophageal adenocarcinoma (EAC)
Intervention	NIVO+Hyal SC
Comparators	NIVO IV
Time horizon	Baseline + 3-year forecast period
Discounting	No discounting applied
Scenario analyses	Scenario A: NIVO dose using a weight-based approach and no wastage Scenario B: Healthcare perspective Scenario C: Healthcare perspective for chair time & HCP time
Costs	Base case: Drug costs Scenario analysis B and C: Base case costs in addition to drug administration costs, and AE management costs
Outcomes	Total costs in the "world with NIVO+Hyal SC" and "world without NIVO+Hyal SC" & incremental budget impact Scenario analysis C: Chair time and HCP time & incremental difference

AE: adverse event; CRC: colorectal cancer; EAC: esophageal adenocarcinoma; GC: gastric cancer, GEJC: gastroesophageal junction cancer; HCP: healthcare practitioner; Hyal: hyaluronidase; IV: intravenous; NIVO: nivolumab; NSCLC: non-small cell lung cancer; RCC: renal cell carcinoma; SC: subcutaneous; SCCHN: squamous cell carcinoma of the head and neck; TKI: tyrosine kinase inhibitor; UC: urothelial carcinoma.

Results

Eligible population

- The total number of NIVO+Hyal SC-eligible patients in Canada was estimated to be 5,895, 6,013, and 6,132 patients in years 1, 2, and 3, respectively.
- For all indications, the number of patients on NIVO IV and NIVO+Hyal SC in the "scenario with NIVO+Hyal SC" scenario were:
  - NIVO IV: 5,178, 4,552, and 3,896 patients for years 1, 2, and 3, respectively
  - NIVO+Hyal SC: 718, 1,460, and 2,236 patients for years 1, 2, and 3, respectively

Base case results - Public Drug Plan perspective

- In the "reference scenario", the drug acquisition costs were estimated to sum up at $575,545,080 in year 1, $586,997,221 in year 2, and $598,677,236 in year 3, amounting to a 3-year total drug acquisition costs of $1,761,219,538.
- In the "scenario with NIVO+Hyal SC", the drug acquisition costs were estimated to be $567,296,622 in year 1, $570,219,264 in year 2, and $572,985,454 in year 3, amounting to a 3-year total drug acquisition costs direct drug cost of $1,710,501,340.

Base case incremental budget impact

- From the base case Public Drug Plan perspective, the incremental budget impact of NIVO+Hyal SC was estimated at -$8,248,458 in year 1, -$16,777,958 in year 2, and -$25,691,782 in year 3.
- Across all indications, the cumulative 3-year incremental budget impact was estimated to be -$50,718,198.
- A total of 4,414 patients were estimated to receive NIVO+Hyal SC in Canada across 3 years with 36% of eligible NIVO IV patients having switched to SC by year 3.

Table 2. Base case and scenario results by year in Canada

All indications	Year 1	Year 2	Year 3	Total
SC-eligible patients	5,895	6,013	6,132	18,040
SC-treated patients	718	1,460	2,236	4,414
Base case				
Costs reference scenario	$575,545,080	$586,997,221	$598,677,236	$1,761,219,538
Costs scenario with NIVO+Hyal SC	$567,296,622	$570,219,264	$572,985,454	$1,710,501,340
Incremental costs	**-$8,248,458**	**-$16,777,958**	**-$25,691,782**	**-$50,718,198**
Scenario A - Weight-based only				
Costs reference scenario	$552,051,469	$563,036,136	$574,239,376	$1,689,326,981
Costs scenario with NIVO+Hyal SC	$547,010,056	$552,781,822	$558,536,986	$1,658,328,863
Incremental costs	**-$5,041,413**	**-$10,254,315**	**-$15,702,390**	**-$30,998,118**
Scenario B - Healthcare perspective				
Costs reference scenario	$599,231,370	$611,154,819	$623,315,520	$1,833,701,709
Costs scenario with NIVO+Hyal SC	$589,176,082	$590,701,614	$591,995,912	$1,771,873,608
Incremental costs	**-$10,055,288**	**-$20,453,205**	**-$31,319,608**	**-$61,828,100**
Scenario C - Chair time and HCP time				
Chair time reference scenario	46,793 hours	47,724 hours	48,674 hours	143,191 hours
Chair time scenario with NIVO+Hyal SC	41,855 hours	37,679 hours	33,293 hours	112,828 hours
Chair time saved	**4,938 hours**	**10,045 hours**	**15,381 hours**	**30,363 hours**
HCP time reference scenario	184,786 hours	188,462 hours	192,212 hours	565,460 hours
HCP time scenario with NIVO+Hyal SC	174,435 hours	167,405 hours	159,970 hours	501,810 hours
Incremental HCP time	**10,351 hours**	**21,057 hours**	**32,243 hours**	**63,650 hours**

HCP: healthcare practitioner; Hyal: hyaluronidase; NIVO: nivolumab; SC: subcutaneous.

Scenario analyses

- In addition to the drug acquisition costs in the base case, three scenario analyses were implemented:
  - The dose of NIVO IV was assumed to be weight-based for all indications for which this was applicable. Full vial sharing was allowed (no wastage)
  - A broader healthcare perspective with additional costs such as drug administration costs (including cost of provider's time) and AE management costs
  - Consideration of chair time and HCP time

Scenario A: NIVO dose using a weight-based approach and no wastage

- The first scenario considered a conservative dosing assumption where NIVO IV was dosed as 3.0, 4.5, & 6.0 mg/kg for Q2W, Q3W & Q4W, respectively. Full vial sharing was assumed.
- The resulting budget impact from this broader perspective is presented in **Table 2** and was estimated at -$5,041,413 in year 1, -$10,254,315 in year 2, and -$15,702,390 in year 3.
- The cumulative 3-year incremental budget impact was estimated to be -$30,998,118 (**Table 2**).
- The weight-based NIVO IV dosing sensitivity scenario also demonstrated that the adoption of NIVO+Hyal SC consistently results in drug cost savings.

Scenario B: Healthcare perspective

- The resulting budget impact from this broader perspective was estimated at -$10,055,288 in year 1, -$20,453,205 in year 2, and -$31,319,608 in year 3 (**Table 2**).
- The cumulative 3-year incremental budget impact was estimated to be -$61,828,100 (**Table 2**).

Scenario C - Chair time & HCP time

- The model estimates total time savings for HCPs of 63,540 hours between the scenario with NIVO+Hyal SC and the reference scenario, and considered nurses, pharmacists, pharmacy technicians, and physicians (**Table 2**).
- The chair time saved for patients is estimated to be 26 minutes per dose received, resulting in total savings of 30,363 hours across indications in Canada (**Table 2**).

Results per province

Results per province for the base case and the three scenarios are presented in **Table 3**.

Table 3. Three-year incremental impact for base case and per scenario in Canada and by province

All indications	3-year incremental impact	
Base case		
Canada*	-$50,718,198	
Alberta	-$5,785,722	
British Columbia	-$7,188,302	
Prince Edward Island	-$222,202	
Manitoba	-$1,765,296	
New Brunswick	-$1,063,936	
Nova Scotia	-$1,353,428	
Newfoundland and Labrador	-$693,392	
Ontario	-$19,944,108	
Quebec	-$11,108,681	
Saskatchewan	-$1,443,892	
Scenario A - NIVO dose using a weight-based approach and no wastage		
Canada*	-$30,998,118	
Alberta	-$3,536,137	
British Columbia	-$4,393,371	
Prince Edward Island	-$135,806	
Manitoba	-$1,078,919	
New Brunswick	-$650,260	
Nova Scotia	-$827,193	
Newfoundland and Labrador	-$423,790	
Ontario	-$12,189,507	
Quebec	-$6,789,441	
Saskatchewan	-$882,483	
Scenario B - Healthcare perspective		
Canada*	-$61,828,100	
Alberta	-$7,225,397	
British Columbia	-$8,976,985	
Prince Edward Island	-$277,493	
Manitoba	-$2,204,559	
New Brunswick	-$1,328,677	
Nova Scotia	-$1,690,204	
Newfoundland and Labrador	-$865,931	
Ontario	-$24,906,848	
Quebec	-$12,362,453	
Saskatchewan	-$1,803,179	
Scenario C - Chair time & HCP time	**3-years Chair time saved (in hours)**	**3-years HCP time saved (in hours)**
Canada*	30,363	63,650
Alberta	3,464	7,261
British Columbia	4,303	9,021
Prince Edward Island	133	279
Manitoba	1,057	2,215
New Brunswick	637	1,335
Nova Scotia	810	1,699
Newfoundland and Labrador	415	870
Ontario	11,940	25,030
Quebec	6,650	13,941
Saskatchewan	864	1,812

*Canada is the sum of all presented provinces and additional territories which are not presented in the table.
HCP: healthcare practitioner; NIVO: nivolumab.

Conclusion

- The SC formulation has the potential to transform and substantially improve cancer care & healthcare system efficiencies in Canada.
- The adoption of NIVO+Hyal SC would also drive significant savings to the payer's drug budget.
- NIVO+Hyal SC represents a paradigm evolution regarding the optimization of healthcare resources beyond drug acquisition costs, specifically, it reduces chair time, reduces preparation and monitoring time, and allows for greater human resource flexibility, easing the burden in a strained healthcare system, especially when considering the large patient volume.
- In the clinical trial setting, patients generally preferred SC to IV administration for NIVO, further demonstrating its value beyond drug cost savings and gains in system efficiencies.
- Additional real-world studies would further validate these findings.

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