Parallel Scientific Advice from NICE and CADTH: Would One Submission Fit All?

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OBJECTIVES

- To assess the similarities and differences in the decision problem for National Institute for Health and Care Excellence and Canadian Agency for Drugs and Technologies in Health oncology appraisals for the same technology-indication pairing and the subsequent methodological preferences of each of these Health Technology Assessment bodies.
- To use this information to understand the potential challenges in offering parallel scientific advice across these different markets.

BACKGROUND

- Scientific advice is a confidential, fee-based consultancy service offered by some national Health Technology Assessment (HTA) bodies to help manufacturers develop the evidence required for the future HTA of their therapies. Through scientific advice, manufacturers can engage early and directly with national HTA bodies and receive expert advice on their clinical and economic evidence generation plans.[1]
- In February 2019, the National Institute for Health and Care Excellence (NICE) announced a collaboration with the Canadian Agency for Drugs and Technologies in Health (CADTH) to offer parallel scientific advice to pharmaceutical companies across both the English and Canadian markets.[2]
- In recognition of the similarities in the HTA processes between NICE and CADTH, the collaboration aims to provide manufacturers with simultaneous scientific advice through a single, streamlined process **(see Information Box: Parallel Scientific Advice from NICE and CADTH)**.[2]

METHODS

- NICE technology appraisals (TAs) for oncology therapies with final guidance published between January 2017 and April 2019 were identified from the NICE and CADTH websites.
- Where the same therapy and indication had been appraised by both NICE and CADTH's pan-Canadian Oncology Drug Review (pCODR), the publicly available appraisal documents were downloaded and reviewed.
- Details of the decision problem (population, intervention, comparator(s)), key sources of clinical evidence, economic modelling approach (model structure and use of economic subgroups) and final reimbursement recommendations were extracted.

RESULTS

- A total of 82 relevant NICE TAs were identified, for which 54 (65.9%) had a technology-indication pair that had also been appraised by the pCODR.
- In 11/54 (20.4%) appraisal pairs, the population, key sources of clinical evidence, comparators and economic modelling approach were the same across both NICE and CADTH appraisals.
- However, in several cases, there were substantial differences in the approaches taken in submissions to NICE vs those to CADTH, as well as differences in the resulting recommendations.
- In 4/54 (7.4%) appraisal pairs the population differed and in 19/54 (35.2%) appraisal pairs the comparators differed. In 12/54 (22.2%) appraisal pairs the key sources of clinical evidence on the intervention and/or comparators differed, and in 17/54 (31.5%) appraisal pairs, the economic modelling approach differed **(Figure 1)**.
- Different reimbursement recommendations were reached in 11/54 (20.4%) appraisal pairs; in six cases, the technology received a positive recommendation from NICE but not from CADTH, whereas in five cases the technology received a positive recommendation from CADTH but not from NICE.
- **Case Studies 1 and 2** provide examples of submissions to NICE and CADTH for the same technology-indication pairing where both the approach (in terms of the comparators, clinical trials informing the economic model, and/or economic modelling approach) and ultimate recommendations differed substantially.

CONCLUSIONS

- Despite similarities in the HTA processes of both England and Canada, less than one quarter of appraisals analysed for the same technology-indication pairing were found to be aligned in terms of the population, intervention, comparators and economic modelling approach.
- The most common difference between appraisals was the choice of comparators, potentially highlighting substantial differences in clinical practice and/or strategic considerations from manufacturers within these two countries.
- Following the establishment of parallel scientific advice from NICE and CADTH, the notable differences identified between appraisals for the same technology-indication pairing highlight sources of potential difficulty in offering parallel scientific advice across these different markets.
- Effective parallel advice therefore needs to ensure that manufacturers understand where NICE and CADTH preferences may necessitate divergent approaches.
- It is encouraging to see the process for NICE and CADTH parallel advice acknowledge this potential need for separate advice between the two bodies.[2]

Information box: parallel scientific advice from NICE and CADTH[2,3]

Aim	• To provide comprehensive and practical advice to manufacturers on their evidence generation plans, in order to meet the requirements of the English and Canadian healthcare systems.
Process	• Products in the early stages of drug development are eligible for advice; i.e. those that are yet to be investigated in phase 3 or other pivotal trials. • Manufacturers submit the same briefing book to NICE and CADTH, although two HTA body-specific questions are also permitted. • A joint face-to-face meeting with the HTA bodies subsequently takes place.
Outcome	• The manufacturer receives separate advice reports from both NICE and CADTH in addition to a summary of alignment between the two HTA bodies. • There is an opportunity for the manufacturer to submit clarification questions on the reports.
Fees	• Fees are charged by both NICE and CADTH based on the complexity and scope of the briefing book.

CADTH: Canadian Agency for Drugs and Technologies in Health; HTA: Health Technology Assessment; NICE: The National Institute for Health and Care Excellence.

1 Differences in the decision problem and recommendations between NICE and CADTH appraisals for the same technology-indication pairing

35.2%

In 35.2% of appraisal pairs, the comparators differed

22.5%

In 22.5% of appraisal pairs, the key sources of clinical evidence differed

31.5%

In 31.5% of appraisal pairs, the economic modelling approach differed

20.4%

In 20.4% of appraisal pairs, the reimbursement decision differed

7.4%

In 7.4% of appraisal pairs, the population[a] differed

[a]Whilst all appraisal pairs were matched for the broad indication, the population was considered to differ if different subpopulations within that indication (e.g. a requirement for specific prior therapies or patients at a specific line of therapy) were presented in the decision problem between the NICE and CADTH appraisals. CADTH: Canadian Agency for Drugs and Technologies in Health; NICE: The National Institute for Health and Care Excellence.

Case study 1	Daratumumab for multiple myeloma	
	TA510 March 2018	**pCODR 10079** December 2016
Recommendation	✓ (Cancer Drugs Fund)	✗
Population	Relapsed and refractory multiple myeloma	Relapsed and refractory multiple myeloma
Intervention	Daratumumab	Daratumumab
Comparators	• Pomalidomide plus dexamethasone • Panobinostat plus bortezomib plus dexamethasone	• Pomalidomide plus dexamethasone • **Cyclophosphamide plus bortezomib plus dexamethasone** • **High dose dexamethasone**
Clinical trials informing economic model	• Intervention – MMY2002 and GEN501 • Comparators – MM-003 and PANORAMA-2	• Intervention – MMY2002 and GEN501 • **Comparators – international chart review**
Economic modelling approach	• 4-state partitioned survival model • No economic subgroup analyses presented	• **3-state partitioned survival model** • No economic subgroup analyses presented

Case study 2	Blinatumomab for acute lymphoblastic leukaemia	
	TA450 June 2017	**pCODR 10064** April 2016
Recommendation	✓	✗[a]
Population	Relapsed or refractory precursor B-cell acute lymphoblastic leukaemia	Relapsed or refractory precursor B-cell acute lymphoblastic leukaemia
Intervention	Blinatumomab	Blinatumomab
Comparators	• FLAG-IDA	• **Hyper-CVAD**
Clinical trials informing economic model	• Intervention and comparator – TOWER	• **Intervention – MT103-211** • **Comparator – Study 20120310 (with statistical adjustment)**
Economic modelling approach	• 3-state partitioned survival model • Economic subgroup analyses presented	• **4-state partitioned survival model** • **No economic subgroup analyses presented**

Text and icons in **purple** highlight differences between the two appraisals. [a]Blinatumomab was not recommended by CADTH for the treatment of adult patients with Philadelphia chromosome negative relapsed or refractory B precursor acute lymphoblastic leukaemia and who have had only one prior systemic therapy. However, blinatumomab was recommended for the treatment of adult patients with Philadelphia chromosome negative relapsed or refractory B precursor acute lymphoblastic leukaemia and who have had at least two prior lines of systemic therapy, conditional on cost-effectiveness being improved to an acceptable level. FLAG-IDA: fludarabine, cytarabine, granulocyte-colony stimulating factor and idarubicin; hyper-CVAD: hyperfractionated cyclophosphamide, vincristine, doxorubicin (adriamycin) and dexamethasone; pCODR: pan-Canadian Oncology Drug Review; TA: technology appraisal.

References

1. National Institute for Health and Care Excellence 2019. Scientific Advice. Available at: https://www.nice.org.uk/about/what-we-do/life-sciences/scientific-advice [Last accessed 16 September 2019]; **2.** Canadian Agency for Drugs and Technologies in Health 2019. New Opportunity: Parallel Scientific Advice From CADTH and NICE. Available at: https://cadth.ca/news/new-opportunity-parallel-scientific-advice-cadth-and-nice [Last accessed 16 September 2019]; **3.** Evidera 2019. Policy Trends Update: CADTH Launches Parallel Scientific Advice Programs with NICE and Health Canada. Available at: https://www.evidera.com/policy-trends-update-cadth-launches-parallel-scientific-advice-programs-with-nice-and-health-canada/ [Last accessed 16 September 2019].

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