Characterizing files reviewed through the CDA-AMC Complex Review Process: 2020-2023

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Background and Objectives

- The complex review process, introduced by Canada's Drug Agency (CDA-AMC; formerly CADTH) in November 2021, was designed to evaluate innovative health technologies that face unique clinical and ethical challenges, such as drugs for rare diseases.
- Per the CDA-AMC Procedures for Reimbursement Reviews[1], drugs eligible for review through the complex review process include:
  - cell and gene therapies;
  - drugs that are first-in-class;
  - drugs reviewed through one of Health Canada's expedited pathways (i.e., priority review or advance consideration under NOC/c);
  - and drugs that have an undefined place in therapy."
- It is crucial for stakeholders to understand the application of this process and implications for the assessment of health technologies.
- The objective of this analysis was to characterize uptake of the complex review process, the types of drugs being reviewed through this mechanism, evidence packages submitted for CDA-AMC review, and outcomes of the CDA-AMC assessment.

Methods

Study Design

- Retrospective descriptive analysis.

Search and Screening

- The CDA-AMC Reimbursement Reviews database was used to identify all reviews with final recommendations dated between 2020 to 2023 and Schedule E fees (complex reviews).

Data Extraction

- Data were extracted by a single reviewer and validated by a second reviewer.
- Extracted data included identifying characteristics of the file (brand name, generic name, indication), Health Canada review type, summary recommendation, the number of clinicians consulted, clinical evidence submitted for review (study design of pivotal trials, OLEs, ITCs, RWE), economic characteristics (cost per year or cycle, CDA-AMC reanalyzed ICER, recommended price reduction), and ethical/implementation considerations.
- Characteristics of the reviews were qualitatively analyzed. The data extraction was conducted in Microsoft® Excel (Version 2407).

Results

- Between 2020-2023, there were 17 files (10 oncology, 7 non-oncology) of 15 unique drugs reviewed through the complex review process. This represents 6% (17/275) of all CDA-AMC Reimbursement Reviews during that period.
- 16 of the 17 files received a reimburse with clinical criteria and/or conditions (i.e., positive) recommendation.
- Of the 15 unique drugs, there were 6 cell therapies (ABECMA, BREYANZI, CARVYKTI, KYMRIAH, TECARTUS, YESCARTA), 2 gene therapies (LUXTURNA, ZOLGENSMA), 1 radiopharmaceutical (PLUVICTO), and 1 RNA interference therapeutic (OXLUMO).
- 5 reviews (29%) met at least 1 of the criteria for complex reviews, 9 reviews (53%) met at least 2, and 3 reviews (18%) met at least 3. It appears that no drugs were reviewed through the complex review process solely due to an undefined place in therapy.

Table 1: Eligibility Criteria Met by Files Reviewed Through the CDA-AMC Complex Review Process (2020-2023)

Review	Cell/Gene Therapy	First-in-Class*	Health Canada Expedited Pathway	Undefined Place in Therapy**
BREYANZI (Large B-cell lymphoma)	■			
KOSELUGO (Neurofibromatosis type 1)		■		
PLUVICTO (mCRPC)			■	
TRIKAFTA (Cystic fibrosis)			■	
YESCARTA (Follicular lymphoma)	■			
CARVYKTI (Multiple myeloma)	■		■	
IMCIVREE (Bardet-Biedl syndrome)		■	■	
KYMRIAH (Follicular lymphoma)	■		■	
LUXTURNA (Vision loss, inherited retinal dystrophy)	■	■		
OXLUMO (Primary hyperoxaluria type 1)		■	■	
SOHONOS (Fibrodysplasia Ossificans Progressiva)		■	■	
TECARTUS (Acute lymphoblastic leukemia)	■		■	
WELIREG (von Hippel-Lindau disease)		■	■	
YESCARTA (DLBL or high-grade B-cell lymphoma)	■	■		
ABECMA (Multiple myeloma)	■	■	■	
TECARTUS (Mantle cell lymphoma)	■	■	■	
ZOLGENSMA (Spinal muscular atrophy, pediatrics)	■	■	■	
Total	**10/17 (59%)**	**10/17 (59%)**	**12/17 (70%)**	

*For the purposes of this analysis, first in class was defined as per the FDA: First-in-class drugs are ones that use a new and unique mechanism of action for treating a medical condition.
**Undefined place in therapy was not specifically mentioned in any of the reimbursement review reports or recommendations. As this criterium is not defined in the CDA-AMC Procedures, it is unclear which therapies may have been considered to have an undefined place in therapy.

Results

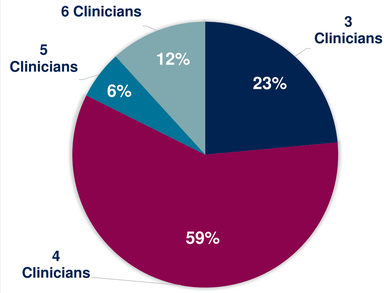

Figure 1: Number of Clinicians Consulted for the Review

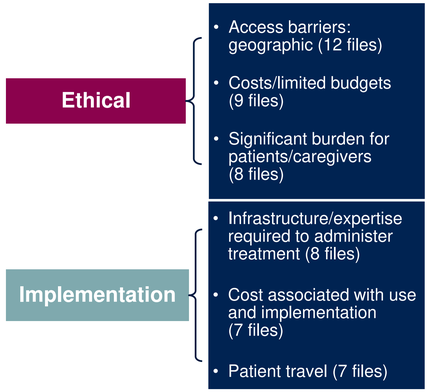

Figure 2: Ethical and Implementation Considerations: Most Common Themes

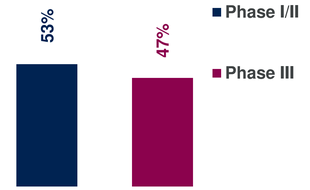

Figure 3: Distribution of Reviews by Pivotal Trial Phase: Phase I/II vs. Phase III

- The pivotal trials were predominantly open-label, multi-centre, and single-arm.
- 9 reviews (53%) included RWE, and 13 reviews (76%) included an ITC.
- For chronic therapies, the annual per patient cost ranged from: $120,000 to $1.7M. For one-time use therapies, the cost ranged from $450,000 to $2.9M per patient.

Discussion

- All reviews aligned with eligibility criteria as stated in the CDA-AMC procedures. Furthermore, all reviews met at least 1 of the following criteria: cell or gene therapy, first-in-class, or reviewed through one of Health Canada's expedited review pathways.
- It is not clear to what extent the reviews may have been considered to meet the undefined place in therapy criterium, as it is not defined in the CDA-AMC Procedures.
- The majority of the complex reviews analyzed involved consultation with >4 clinicians and included open-label, single-arm trials, RWE, and indirect comparative evidence.

Abbreviations CDA-AMC = Canada's Drug Agency – Assessment and Monitoring Committee (formerly CADTH); DLBL = Diffuse large B-cell lymphoma; FDA = Food and Drug Administration; ICER = Incremental cost-effectiveness ratio; ITC = Indirect treatment comparison; mCRPC = Metastatic castration-resistant prostate cancer; NOC/c = Notice of Compliance with Conditions; OLE = Open-label extension; RWE = Real-world evidence; RNA = ribonucleic acid.

References Canada's Drug Agency. (May 2024). CDA-AMC Drug Reimbursement Review Procedures.

2024 CDA-AMC Symposium | Shaw Center, Ottawa
September 4 to 6, 2024

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