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Technology Agency

CADTH Initiatives in DRD, RWE, and RDR: A journey through critical acronyms

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CADTH was established by Canada's federal, provincial, and territorial governments to be a trusted source of independent information and advice for the country's publicly funded health care systems.

Initiatives at CADTH associated with Rare Diseases
(as of November 2023)

"THE ACRONYMS"

1. **RWE**
   Real **W**orld **E**vidence
2. **RDR**
   Rare Disease Registries
3. **DRD PR**
   The DRD **P**ipeline **R**epository
4. **NBS EP**
   The **N**ew**B**orn **S**creening **E**xpert **P**anel
5. **FMEC**
   Formulary **M**anagement **E**xpert **C**ommittee
6. **TLR**
   Time-**L**imited **R**eviews

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1 RWE

Real-World Evidence

- How is CADTH incorporating RWE into Reimbursement Reviews and other assessment tools/products?
- Published Guidelines in May 2022
- Actively working on RWE Standards and Guidelines for RWE that will be used in CADTH technology assessment processes

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2 RDR

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Drug Data Services and Analytics

- CADTH's newest unit
- Established in summer 2023 to support work on Health Canada's Rare Disease Strategy

Inaugural projects:

1. Create a "Registry of Registries" for Rare Diseases
   - Assess the quality and comprehensiveness of data within those registries.
   - Work with registry owners to achieve data completeness and quality improvements so that registries can be 'fit for purpose' for both HTA and regulatory purposes.

2. Registry Standards and Guidelines
   - Establish data standards for registries to be 'fit for purpose' for both HTA and regulatory evaluations

3. Test existing registries in HTA and identify barriers or limitations in data readiness, comprehensiveness, and/or ability to report on relevant outcomes.

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Alignment with other DRD/RWE initiatives under the National DRD Strategy:

CIHI

- Identify and describe the process, barriers, and limitations of linking registry data to CIHI data holdings.
- Use these findings to support registry owners to improve data collection or quality

Government of Canada / Gouvernement du Canada

Health Canada DRD Secretariat
Canadian Drug Agency Transition Office

- Using one or more DRD registries, support a regulatory evaluation using registry data to answer specific regulatory questions.
- Use these findings to support registry owners to improve data collection and/or data quality

Réseau de recherche sur les données de santé du Canada
Health Data Research Network Canada

- Establishing a process by which policymakers, regulatory bodies, P/T's or CADTH can submit queries through HDRN outside of the existing academic/research process.

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3 DRD PR

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DRD Pipeline Review/Repository

- A tool for decision-makers to access for more timely and relevant DRD information to inform planning
- Actively working with F/P/T decision makers on the design and specifications

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4 NBS EP

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NBS EP
NewBorn Screening Expert Panel

- CADTH is convening an expert panel to provide advice on a pan-Canadian approach to newborn screening, key components include establishing a common set of guiding principles and a proposed common approach for updating the list of conditions screened.
- Panel Co-chairs have agreed to participate as well as several other panel members, membership should be finalized by end of year.
- CADTH is also meeting with newborn screening teams within P/T gov'ts to understand current approaches and perspectives

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5 FMEC

Formulary Management Expert Committee (FMEC)

Purpose:

Provide recommendations to drug reviews across the product life span (e.g., drugs at or beyond the loss of exclusivity)

Context:

- Pilot a new expert committee to leverage opportunities to produce tailored reviews as requested by drug plans and to support appropriate use and optimal utilization of drug benefits.
- Provide an innovation sandbox to develop new approaches to review deliberations and provide an opportunity for committee member development.

Approach:

A test-and-learn approach that builds upon the learnings of each review type and deliberation. The phased approach will focus on one review-type at a time in increasing complexity.

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Types of Reviews for FMEC

Non-Sponsored Single Drug Reviews	Streamlined Drug Class Reviews	Therapeutic Reviews
• Provides a review on a single drug that is at or beyond exclusivity but with new evidence to support its use in a previously unfunded indication • Does not include a cost-utility analysis • *Non-Sponsored Reimbursement Review Procedures*	• Provides a review on a class of drugs where new evidence and/or updated pricing (e.g., loss of exclusivity) supports a change in place of therapy • Pools drugs into classes to reduce uncertainty • Leverages well-conducted published network meta-analyses • *Streamlined Drug Class Review Procedures*	• Provides a review on an entire therapeutic area where there is significant interest from payers • Time needed beforehand to develop a network meta-analysis and cost-utility model • To expedite timing, CADTH is looking to partner with NICE, ICER, and ZIN to "exchange" models for the future • *Therapeutic Review Procedures*

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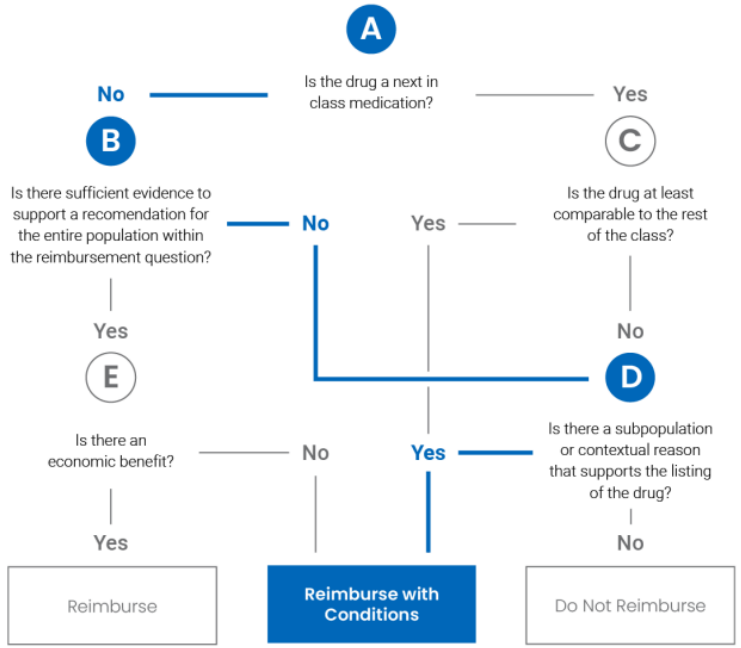
Recommendation Report

Deliberative Framework

Figure 1
Decision Path



NEW –
Increased transparency by publishing:

- Deliberative framework decision path
- Votes
- Dissenting opinion

Decision Summary

Table 1
Why Did FMEC Make This Recommendation?

Decision Node	Vote	Reason
A **Is the drug a next-in-class medication?**	**Yes (1)**	• FMEC acknowledged that there is currently no evidence to inform whether a liquid formulation of rivaroxaban can improve compliance in the treatment of VTE. FMEC also acknowledged that the availability of a liquid formulation does not necessarily meet the criterion for a next-in-class medication.
	No (6)	• FMEC noted that rivaroxaban is not a next-in-class medication. While other direct oral anticoagulants (e.g., apixaban) may be available and used in the pediatric setting, they are not available as a liquid formulation. • FMEC considered that there is a significant unmet need in the treatment of VTE in the pediatric population, especially with options that are more convenient (e.g., oral liquid formulation) and require less monitoring (e.g., no routine bloodwork requirement).
B **Is there sufficient evidence to support a recommendation for the entire population within the reimbursement question?** **Population under consideration for reimbursement:** **Patients aged < 18 years (i.e., term neonates, infants and toddlers, children and adolescents) who require treatment for VTE or prevention of VTE recurrence following ≥ 5 days of initial parenteral anticoagulation treatment**	**Yes (2)**	• FMEC considered that while the benefits of improved compliance are unclear with the oral liquid formulation, the improvement in QoL associated with fewer injections and less monitoring should not be overlooked. These benefits apply to the entire population under consideration.
	No (5)	• FMEC acknowledged that the evidence from the EINSTEIN Jr study informs the efficacy of rivaroxaban for pediatric patients with VTE as compared to LMWH. Within the EINSTEIN Jr study, the population subgroups, including pediatrics patients aged 2 or younger, and those with cancer and/or unprovoked VTE, were small and associated with greater uncertainties in the evidence. Furthermore, preterm neonates were excluded from the study. • FMEC considered the potential differences in efficacy between the oral tablet and oral liquid formulations. The bioequivalence evidence for these formulations was not part of the CADTH review that informed the FMEC deliberation. FMEC acknowledged that such information would reside with the regulatory body (e.g., Health Canada) and is considered as part of the approval requirements.

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6 TLR

What is a Time-Limited Recommendation?

- A TLR is a recommendation to publicly fund a drug or drug regimen for a certain period of time on the condition that:
  - the manufacturer will conduct one or more clinical studies that addresses the uncertainty and
  - CADTH will conduct a future reassessment of the additional evidence.
- CADTH's future reassessment will lead to a final reimbursement recommendation.
- **Launched September 28, 2023**

Initial Assessment Criteria

All the following must be met for consideration for a TLR:

1. **Regulatory review status:** Drug has been reviewed or is under review through Health Canada's NOC/c policy; **AND**
2. **Evidence generation plans:** Phase III trial is being planned and/or conducted in the population of the indication under review and study completion date will not exceed 3 years from the target expert committee meeting date; **AND**
3. **Reassessment commitment:** Sponsor commits to filing reassessment in accordance with CADTH TLR procedures.

CADTH Recommendation

- **Initial Recommendation:**
  - Ultimately up to the expert committee to determine whether a TLR will be issued
  - A TLR will include a TLR-specific reimbursement condition
- **If a TLR is issued:**
  - Status updates on evidence requirements in the CADTH recommendation will be requested twice a year
  - Proactively inform CADTH of any updates to the conduct of the phase III trial
- **Reassessment deliberation:**
  - Recommendation to remove TLR condition only (with or without revisions to other conditions)
  - Recommendation to not reimburse

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