SECTION

HOW DRUGS COME TO CANADA

STEPS IN DRUG APPROVAL AND FUNDING

NF Symposium Presentation
October 29th, 2022

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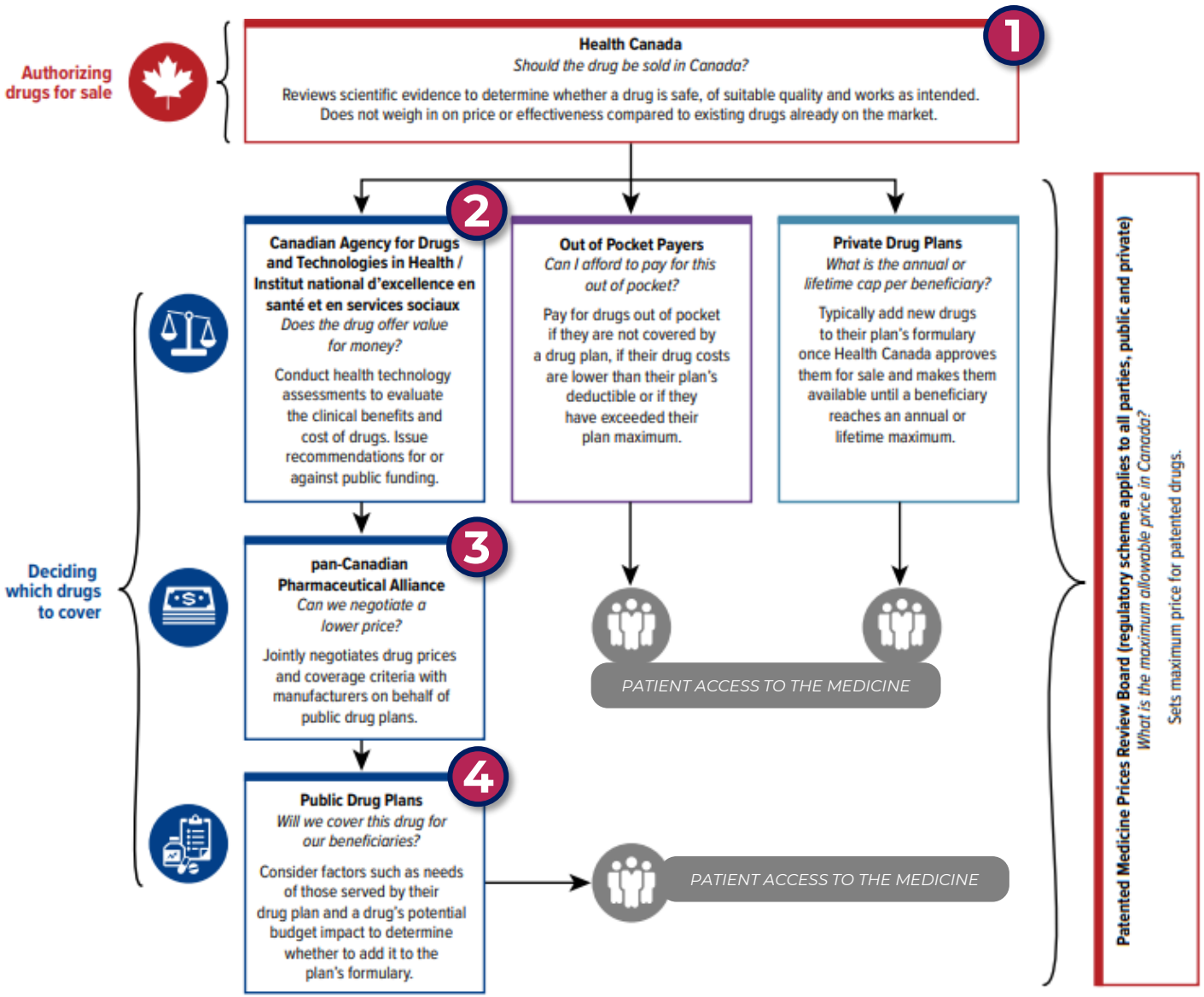
Market Access Manager, Alexion, AstraZeneca Rare Disease Unit

OVERVIEW OF DRUG COVERAGE IN CANADA

Drug approval, review, and public funding in Canada is a **complex and multi-stakeholder process**.

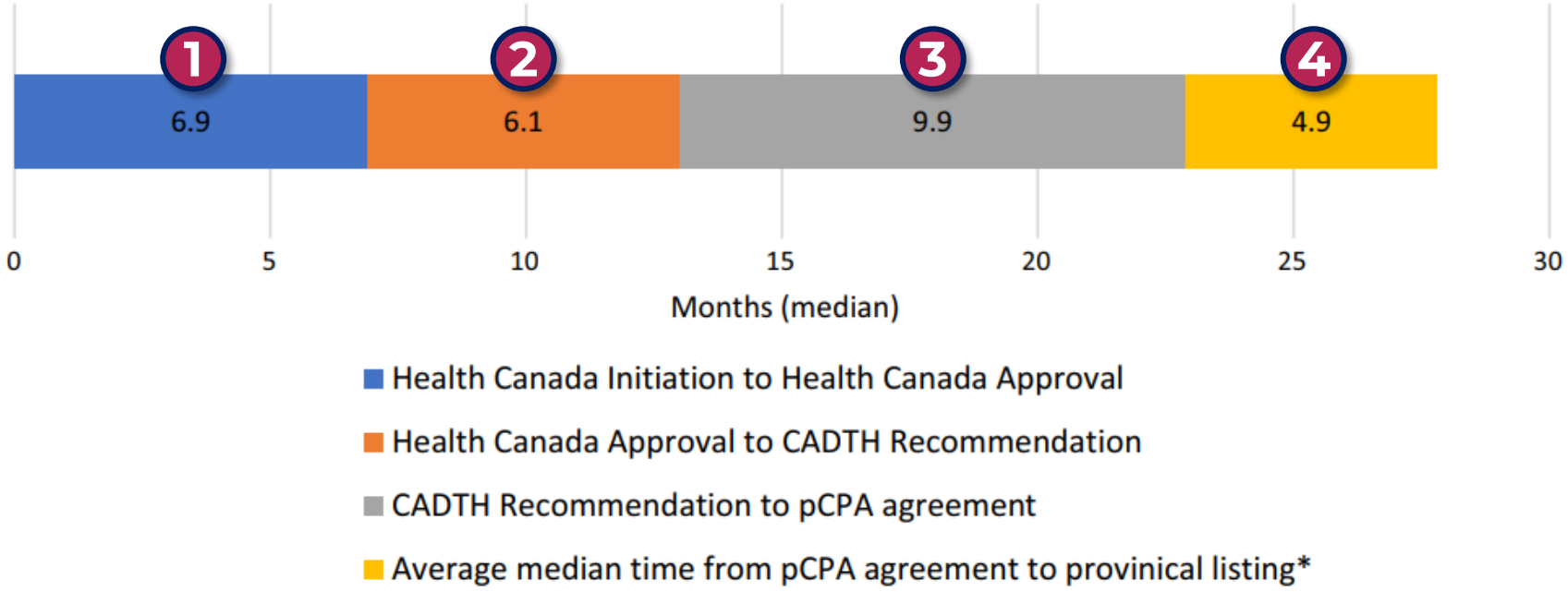
Public payer funding decisions are made only after regulatory approval and HTA review

Private payers conduct their own separate reviews / negotiations



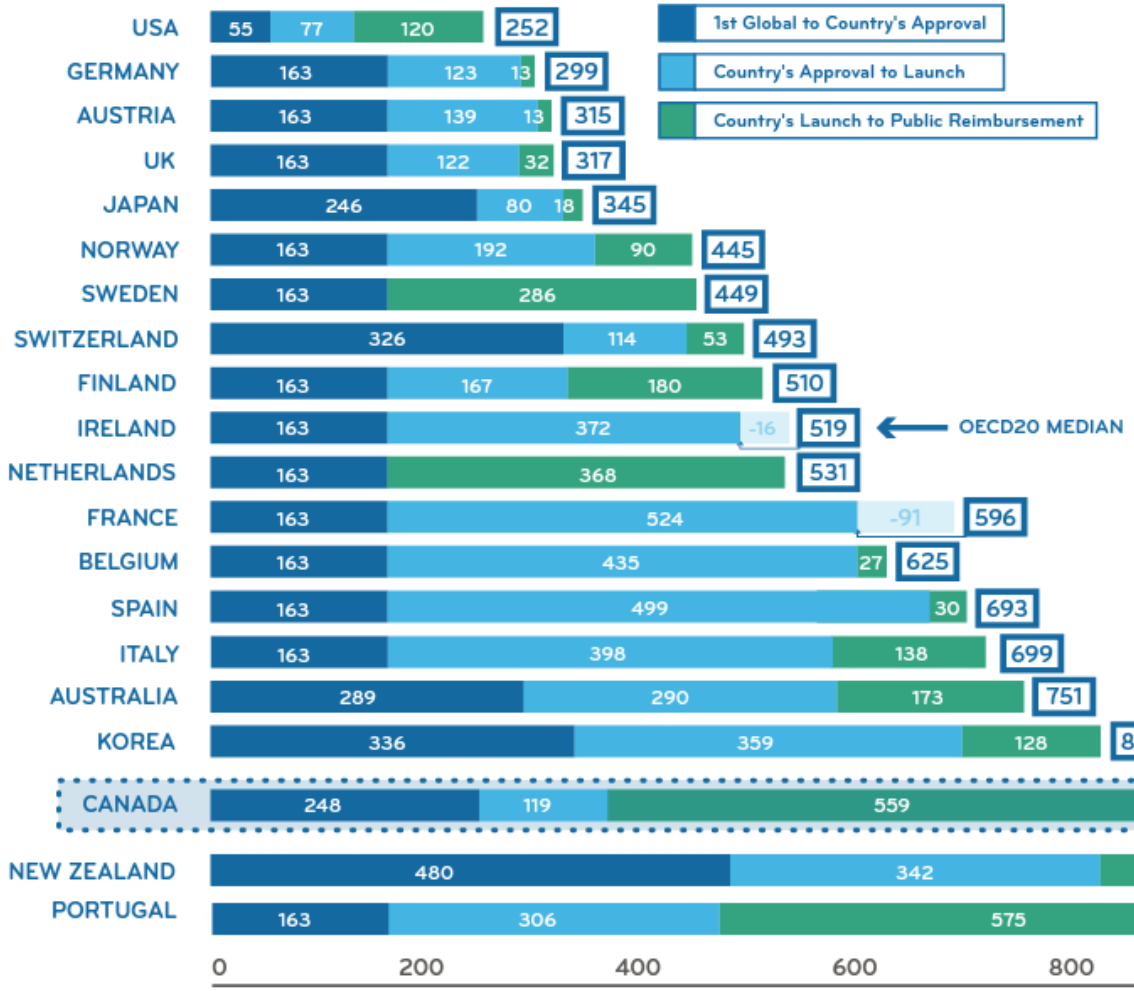
Source: A Prescription for Canada: Achieving Pharmacare for All; https://www.canada.ca/content/dam/hc-sc/images/corporate/about-health-canada/public-engagement/external-advisory-bodies/implementation-national-pharmacare/final-report/final-report.pdf

Considering the large number of stakeholders and steps before a drug is funded and reaches patients, the time to public drug listing can be quite long.



Source: Ward, Leanne Marie, et al. "An international comparative analysis of public reimbursement of orphan drugs in Canadian provinces compared to European countries." Orphanet journal of rare diseases 17.1 (2022): 1-14.

DRUGS COMING TO CANADA: AN OVERVIEW



CANADA IS RELATIVELY QUICK TO APPROVE AND LAUNCH NEW MEDICINES, BUT AMONG THE SLOWEST OF THE OECD20 TO REIMBURSE THEM THROUGH ITS PUBLIC PLANS

Source: EXPLAINING PUBLIC REIMBURSEMENT DELAYS FOR NEW MEDICINES FOR CANADIAN PATIENTS; http://innovativemedicines.ca/wp-content/uploads/2020/07/CADTH-TTL-8.5x11-EN-Final.pdf

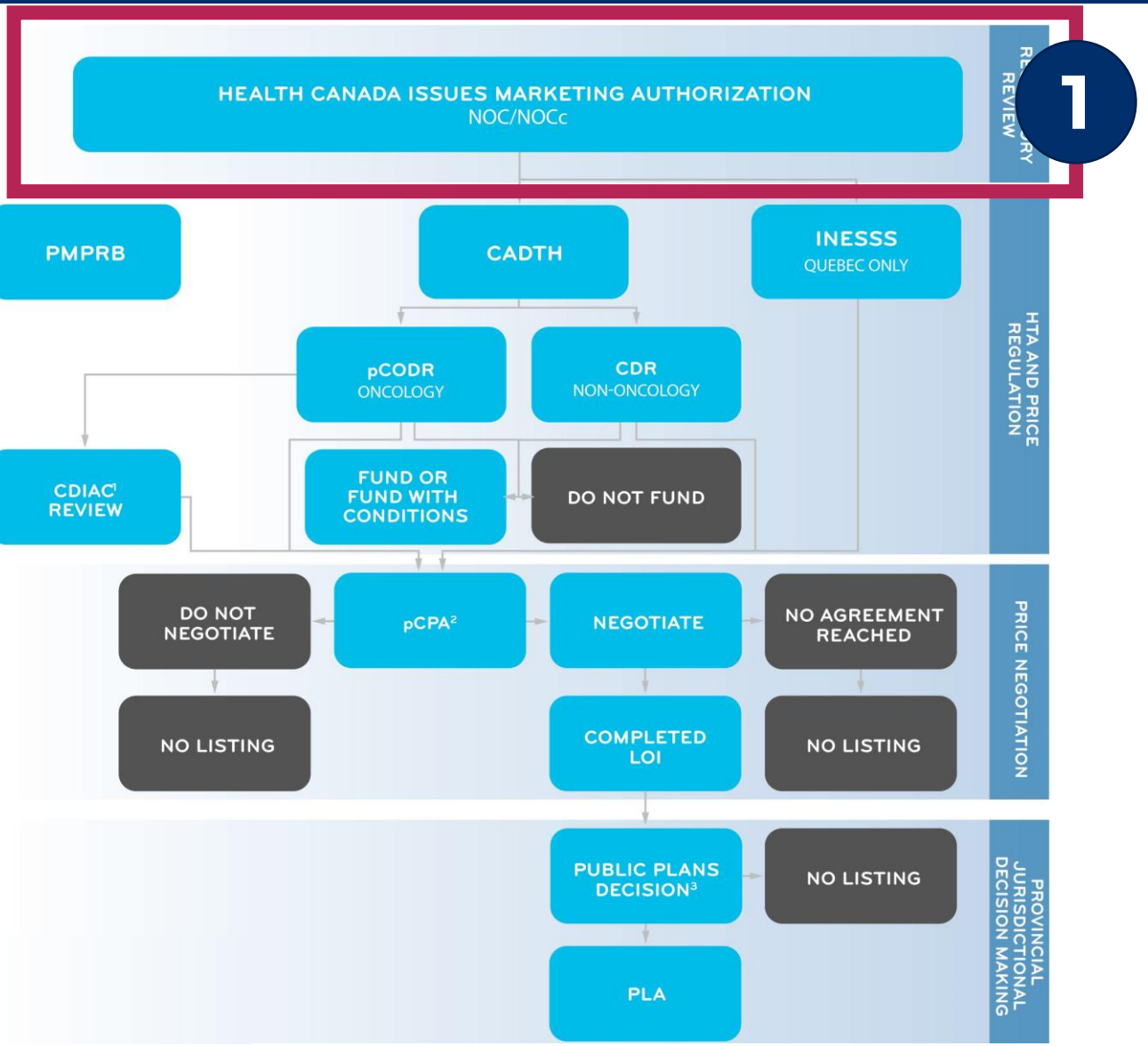
SECTION

DRUG AUTHORIZATION

HEALTH CANADA REVIEW

DRUG APPROVAL AND PUBLIC FUNDING IN CANADA: AN OVERVIEW

Drug approval, review, and public funding in Canada is a complex and multi-stakeholder process.



Source: Salek, Sam, et al. "Factors influencing delays in patient access to new medicines in Canada: a retrospective study of reimbursement processes in public drug plans." Frontiers in Pharmacology 10 (2019): 196.

Health Canada is the Federal department responsible for review and approval for sale of new drugs through the Health Products and Food Branch (HPFB)

HPFB is the national authority that regulates, evaluates and monitors the safety, efficacy, and quality of therapeutic and diagnostic products available to Canadians.

Health Canada does not assess the value / cost of medicines.

When Health Canada reviews a new drug (or new indication), If the conclusion is that the benefits outweigh the risks, the drug is issued a **Notice of Compliance (NOC)**, as well as a Drug Identification Number (DIN) which represents the drug's official approval in Canada.

Health Canada

Source: How Drugs are Reviewed in Canada; https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/fact-sheets/drugs-reviewed-canada.html;

The timelines for a standard review is 300 days.

Canada does not have a "special" review pathway for DRDs.

However, DRDs *may be* eligible for review under the following accelerated pathways:

Notice of Compliance with Conditions (NOC/c)

- ❑ Authorization under the condition that additional studies to verify the clinical benefit are conducted*
- ❑ Review performance standard of 200 days
- ❑ Provides early access to promising new drugs for life-threatening or severely debilitating diseases for which there are currently no available drugs in Canada ***OR*** the target drug provides significant improvement in efficacy or safety

**Once a sponsor provides satisfactory evidence of the drug's clinical effectiveness and all the conditions agreed upon at the outset have been met, the conditions associated with market authorization will be removed in accordance with the NOC/c Policy.*

Priority Review

- ❑ Review performance standard of 180 days
- ❑ Life-threatening or severely debilitating diseases for which there is **substantial evidence** of clinical effectiveness, and which there are currently no available drugs in Canada ***OR*** the target drug provides significant improvement in efficacy or safety

Source: Canada's regulatory approach to drugs for rare diseases: orphan drugs; https://www.canada.ca/en/health-canada/services/licences-authorizations-registrations-drug-health-products/regulatory-approach-drugs-rare-diseases.html

What if a drug is not yet approved in Canada?

Through Health Canada's special access programs (SAP), **HEALTH CARE PROFESSIONALS** may request access to non-marketed drugs and medical devices not yet authorized for sale in Canada, to treat patients with serious or life-threatening conditions.

Access to these drugs is only considered when conventional therapies have failed, are unsuitable, or are unavailable.

These programs are **not** to be used to:

- ❑ promote or encourage the early use of drugs or medical devices
- ❑ conduct research
- ❑ bypass the clinical trial, drug or medical device review process

Source: https://www.canada.ca/en/health-canada/services/drugs-health-products/special-access.html

Useful resources to stay informed on the status of drugs in Canada

Submissions Under Review (SUR) Database

The SUR Lists help to make Health Canada review processes more transparent.

The list is updated monthly, and includes submissions currently under review or completed for:

- new drug submissions
- supplemental new drug submissions for new uses

Drug Product Database (DPD)

The Drug Product Database can be used to find drugs authorized for sale by Health Canada.

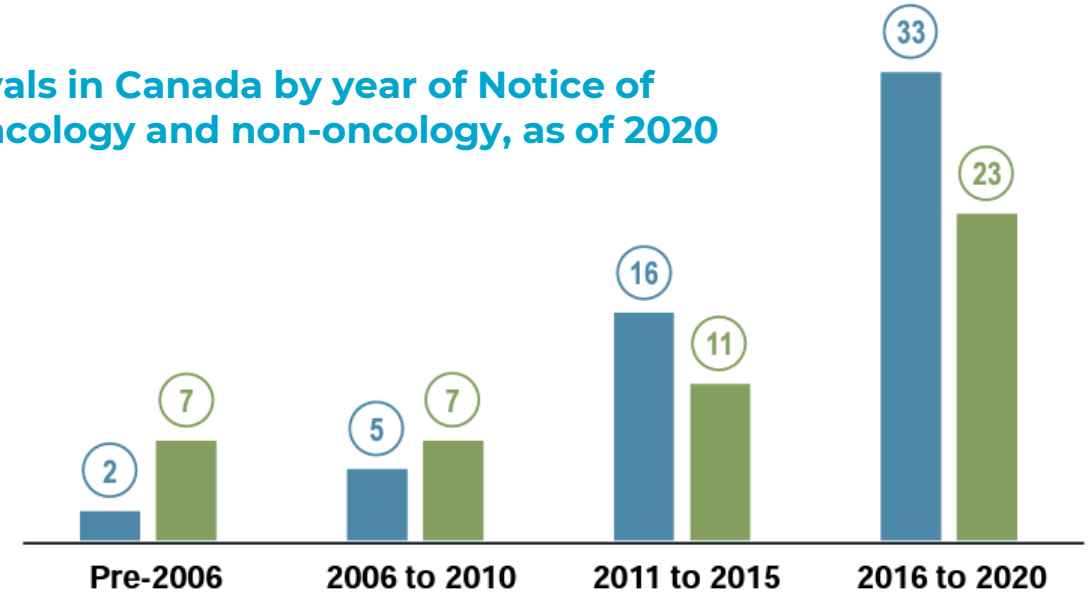
The DPD is updated nightly and includes:

- availability of the drug in Canada
- product monograph (PM) for human drugs

Source: Drug and Health Product Submissions Under Review (SUR), https://www.canada.ca/en/health-canada/services/drug-health-product-review-approval/submissions-under-review.html
Drug Product Database: Access the database, https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html

The pace of approvals of drugs for rare disease is increasing.

DRD approvals in Canada by year of Notice of Compliance, oncology and non-oncology, as of 2020



Cumulative no. of EDRDs

	Pre-2006	2006 to 2010	2011 to 2015	2016 to 2020
Oncology	2	7	23	56
Non-oncology	7	14	25	48
Total	**9**	**21**	**48**	**104**

Source: Expensive Drugs for Rare Diseases Canadian Trends and International Comparisons, 2011–2020, https://www.canada.ca/content/dam/pmprb-cepmb/documents/npduis/analytical-studies/chartbook/edrd-2011-2020/EDRD-Chartbook-2021_EN.pdf

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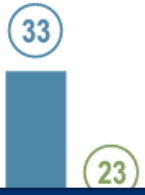

Regulatory approval is only the first step in the drug pathway.

Oncology	2	7	23	56
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Source: Expensive Drugs for Rare Diseases Canadian Trends and International Comparisons, 2011–2020, https://www.canada.ca/content/dam/pmprb-cepmb/documents/npduis/analytical-studies/chartbook/edrd-2011-2020/EDRD-Chartbook-2021_EN.pdf

SECTION

DRUG ASSESSMENT

HTA REVIEW CONDUCTED BY CADTH AND INESSS

DRUG APPROVAL AND PUBLIC FUNDING IN CANADA: AN OVERVIEW

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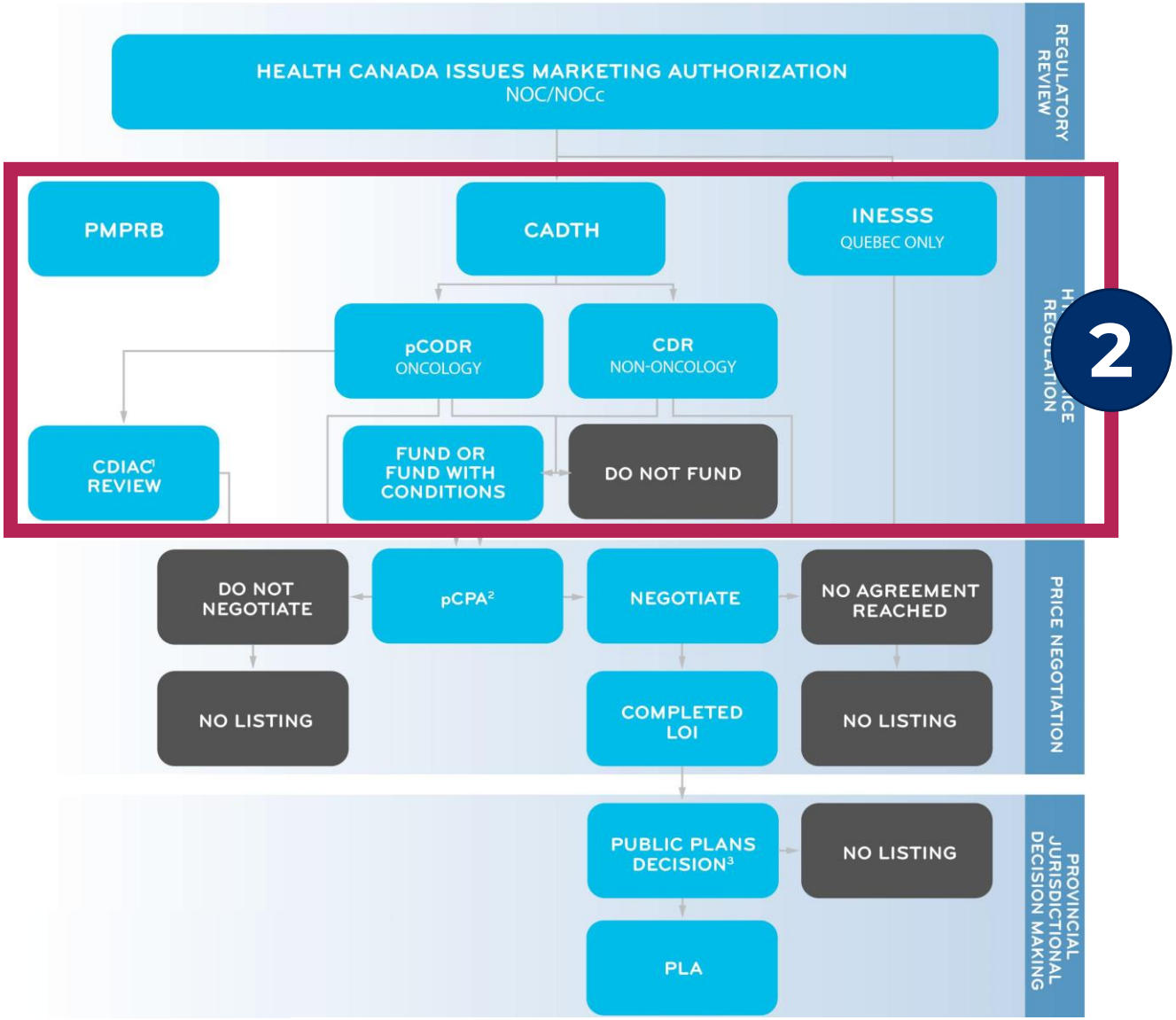
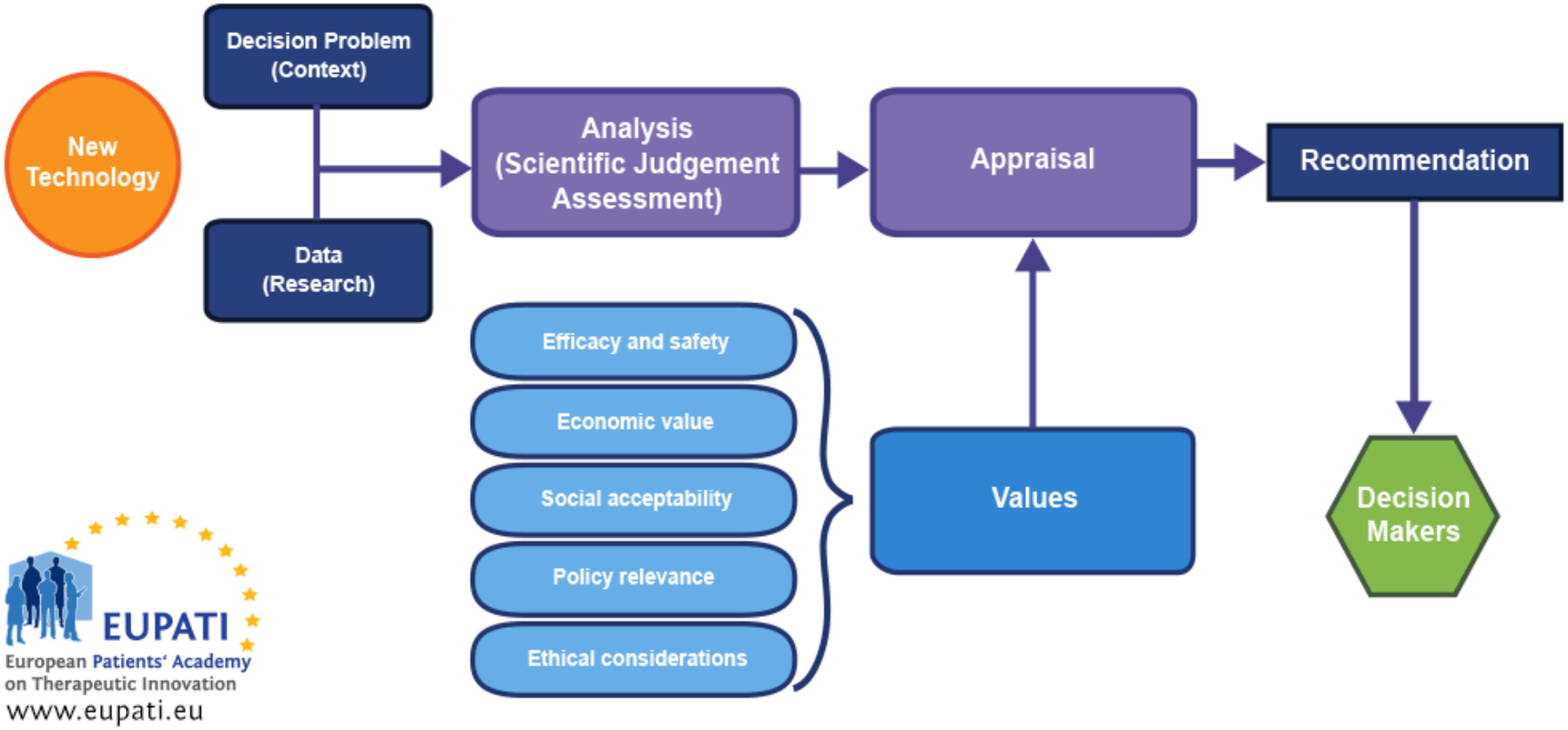


Source: Salek, Sam, et al. "Factors influencing delays in patient access to new medicines in Canada: a retrospective study of reimbursement processes in public drug plans." Frontiers in Pharmacology 10 (2019): 196.

Health Technology Assessment focuses on assessing the evidence and the clinical, economic, and societal value of a new health product.



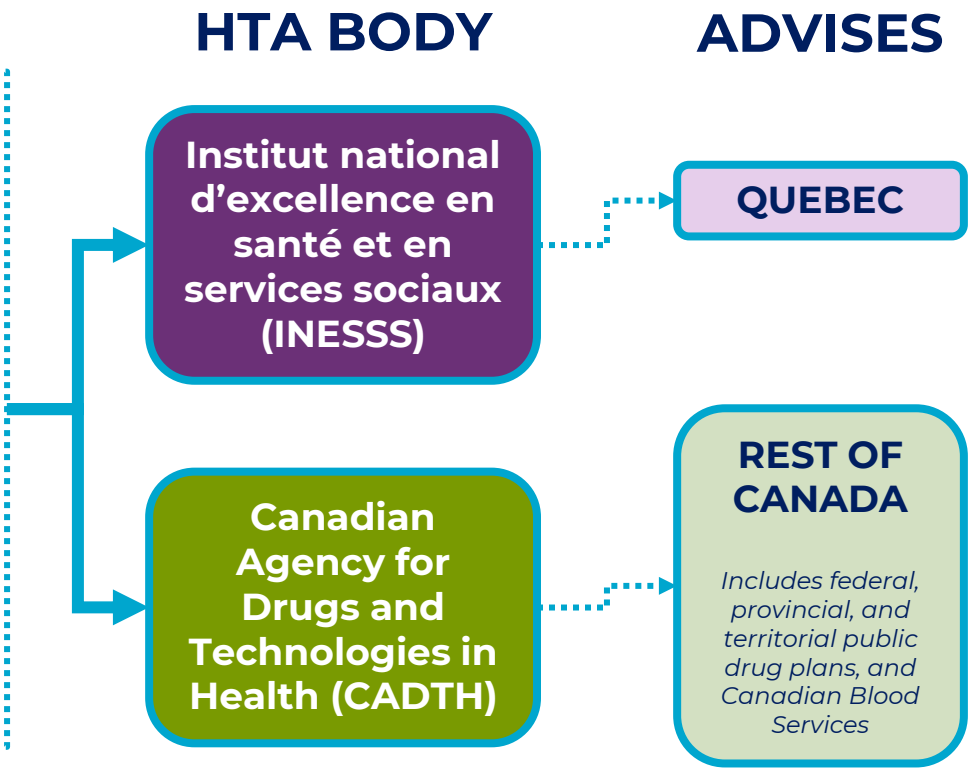
Source: HTA systems in Europe, https://toolbox.eupati.eu/resources/hta-systems-in-europe/

In Canada, drugs must first undergo a Health Technology Assessment to receive a reimbursement recommendation.

Conduct thorough and objective evaluations of the:

- **Clinical Evidence**
- **Economic Evidence**
  - **Includes pharmacoeconomic and budget impact analyses**
- **Patient Perspectives**
- **Clinician Perspectives**
- **Societal Perspective (*INESSS Only*)**

on drugs, and uses these evaluations to provide reimbursement recommendations and advice



Source: CADTH 2022–2025 Strategic Plan; https://strategicplan.cadth.ca/wp-content/uploads/2022/03/cadth_2022_2025_strategic_plan.pdf
ABOUT THE INSTITUT; https://www.inesss.qc.ca/en/about-us/about-the-institut.html

Both INESSS and CADTH can provide three types of recommendations

CADTH

1. Reimburse
2. Reimburse with Clinical Criteria and/or Conditions
3. Do Not Reimburse

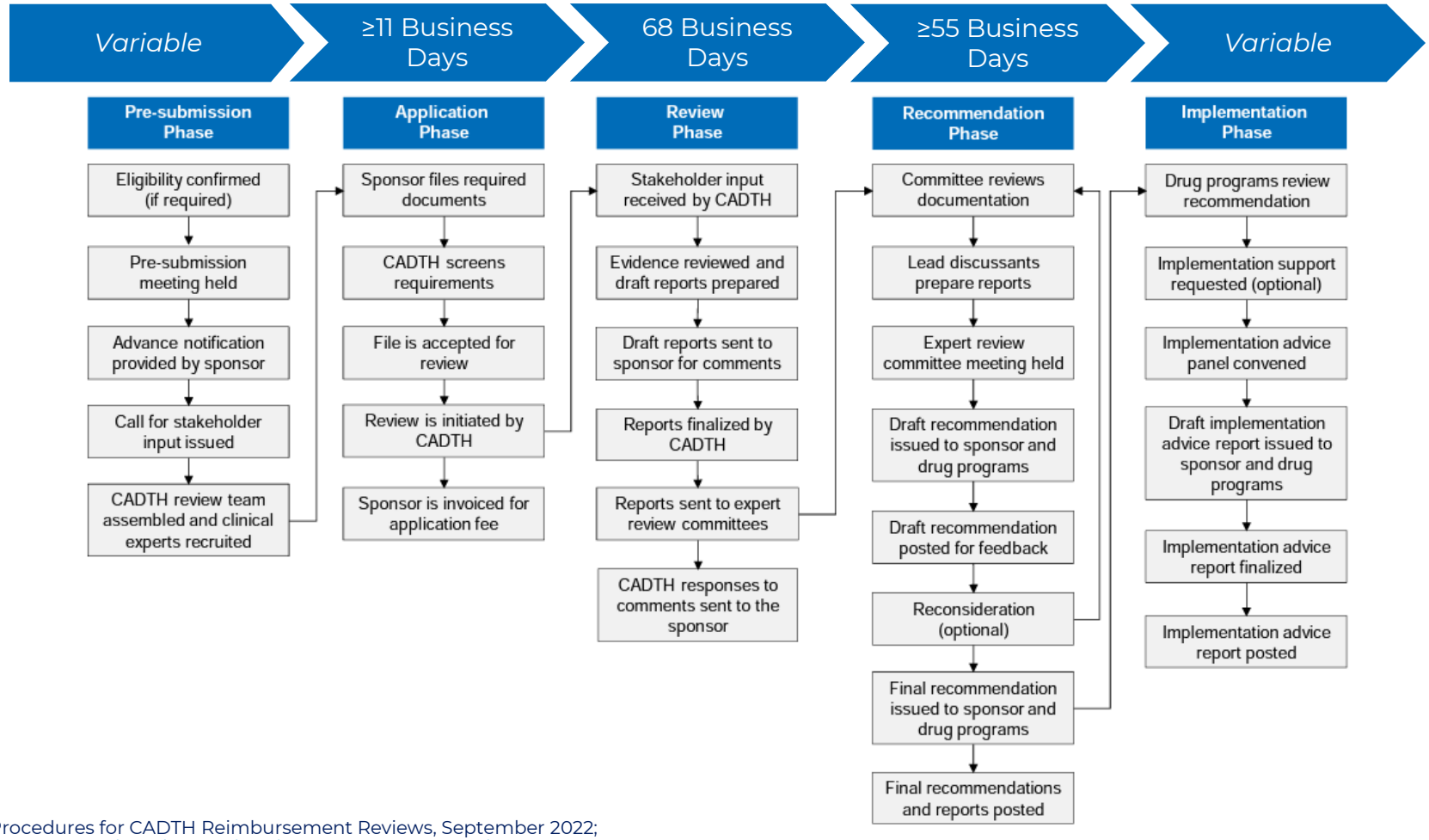
INESSS

1. Listing
2. Conditional Listing (Exceptional Drug / Monitoring / Reduction of Economic Burden)
3. Do Not List

These recommendations are non-binding

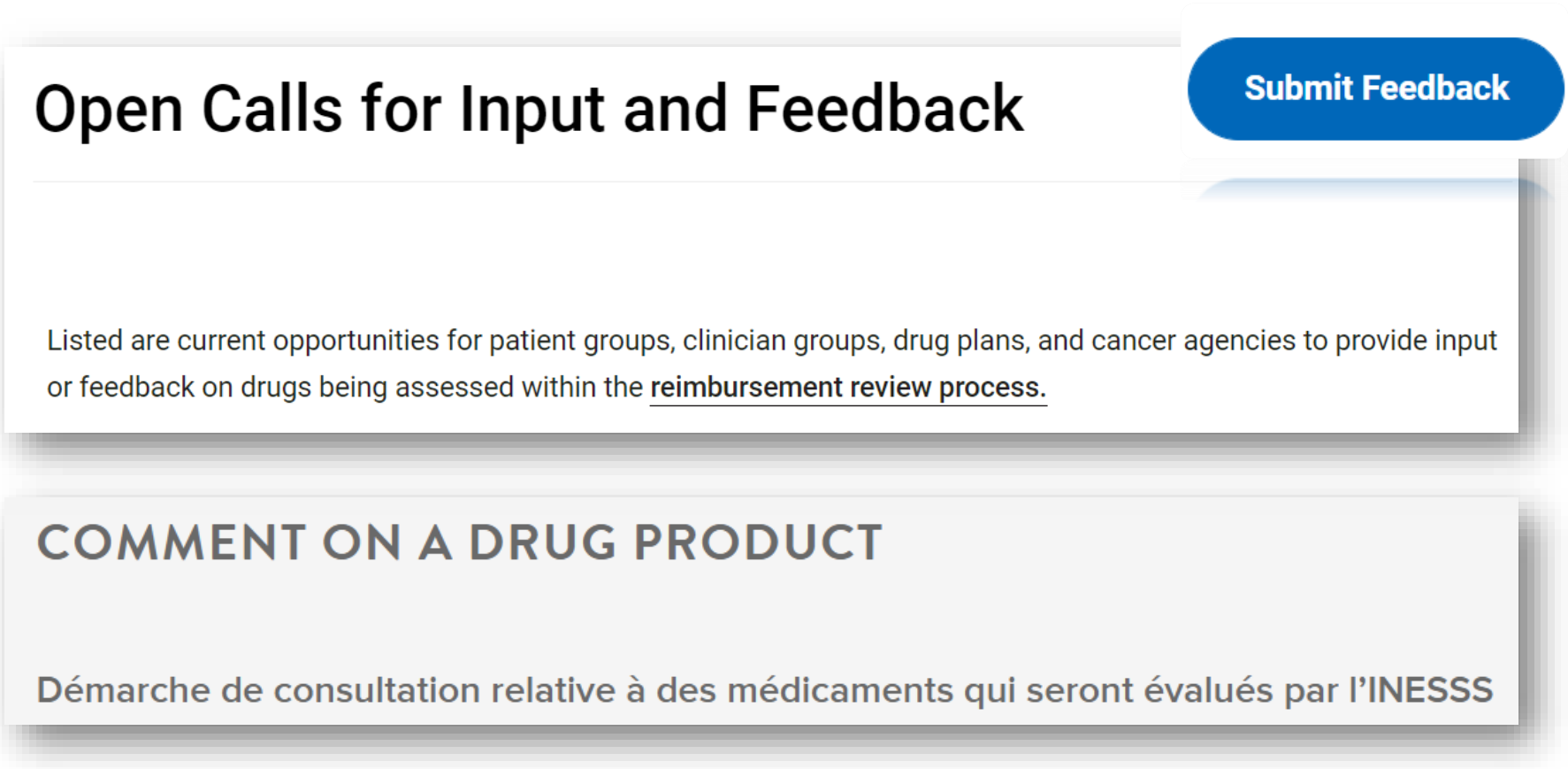
Source: Procedures for CADTH Reimbursement Reviews, September 2022;
https://www.cadth.ca/sites/default/files/Drug_Review_Process/CADTH_Drug_Reimbursement_Review_Procedures.pdf
EVALUATION OF DRUGS FOR LISTING PURPOSES – A CHANGE OF APPROACH,
https://www.inesss.qc.ca/fileadmin/doc/INESSS/Inscription_medicaments/Processus/Evaluation_of_drugs_a_change_of_approach.pdf

The CADTH review process involves many steps and stakeholders. Target for review is ≥134 business days (~190 calendar days)



Source: Procedures for CADTH Reimbursement Reviews, September 2022;
https://www.cadth.ca/sites/default/files/Drug_Review_Process/CADTH_Drug_Reimbursement_Review_Procedures.pdf

Both INESSS and CADTH provide opportunities for patient and clinician input.



Source: Open Calls for Input and Feedback, https://www.cadth.ca/open-calls-input-and-feedback-0
FAIRE UN COMMENTAIRE SUR UN MÉDICAMENT, https://www.inesss.qc.ca/thematiques/medicaments/medicaments-evaluation-aux-fins-dinscription/faire-un-commentaire-sur-un-medicament.html

CADTH does not have a distinct pathway for the review of DRDs.

However, considerations for significant unmet need include disease rarity.

Rarity of condition	• The drug under review is approved by Health Canada for the treatment of a rare disease. Specifically, the condition for which the drug is indicated has the following characteristics: ▪ is life-threatening, seriously debilitating, or both serious and chronic in nature ▪ affects a relatively small number of patients (incidence of fewer than 5 in 10,000, but typically closer to 1 in 100,000) ▪ is often genetically based, onset at birth or early childhood, and leads to a shortened lifespan ▪ places a heavy burden on caregivers and the health care system ▪ is difficult to study because of the small patient population.
Population	• Need is identified on a population or subpopulation basis and not on an individual basis.
Absence of alternatives	• There is an absence of clinically effective drug or non-drug alternative treatments. • Substantial morbidity and mortality exist despite the available drug or non-drug alternative treatments.

Similarly, DRDs may be eligible for a **complex review** which involves greater consultation with clinical experts (e.g., convening a pan-Canadian panel of specialists), greater consideration of non-randomized studies, and examination of potential implementation / ethical issues.

Source: Procedures for CADTH Reimbursement Reviews, September 2022;
https://www.cadth.ca/sites/default/files/Drug_Review_Process/CADTH_Drug_Reimbursement_Review_Procedures.pdf

INESSS carries out its drug evaluation mandate based on five parameters, including societal impact

PARAMETERS

1	2	3	4	5
The therapeutic value.	The reasonableness of the price charged.	The cost-effectiveness ratio of the medication.	Impact of adding the medication to the list on the health of the population and on the other components of the health and social services system.	The advisability of adding the medication to the list with regard to the purpose of the public plan[3].

Whilst a separate process is not available for DRDs, the drug evaluation process makes it possible to consider the reality of new drugs for rare diseases (unmet health need and promise of value).[2]

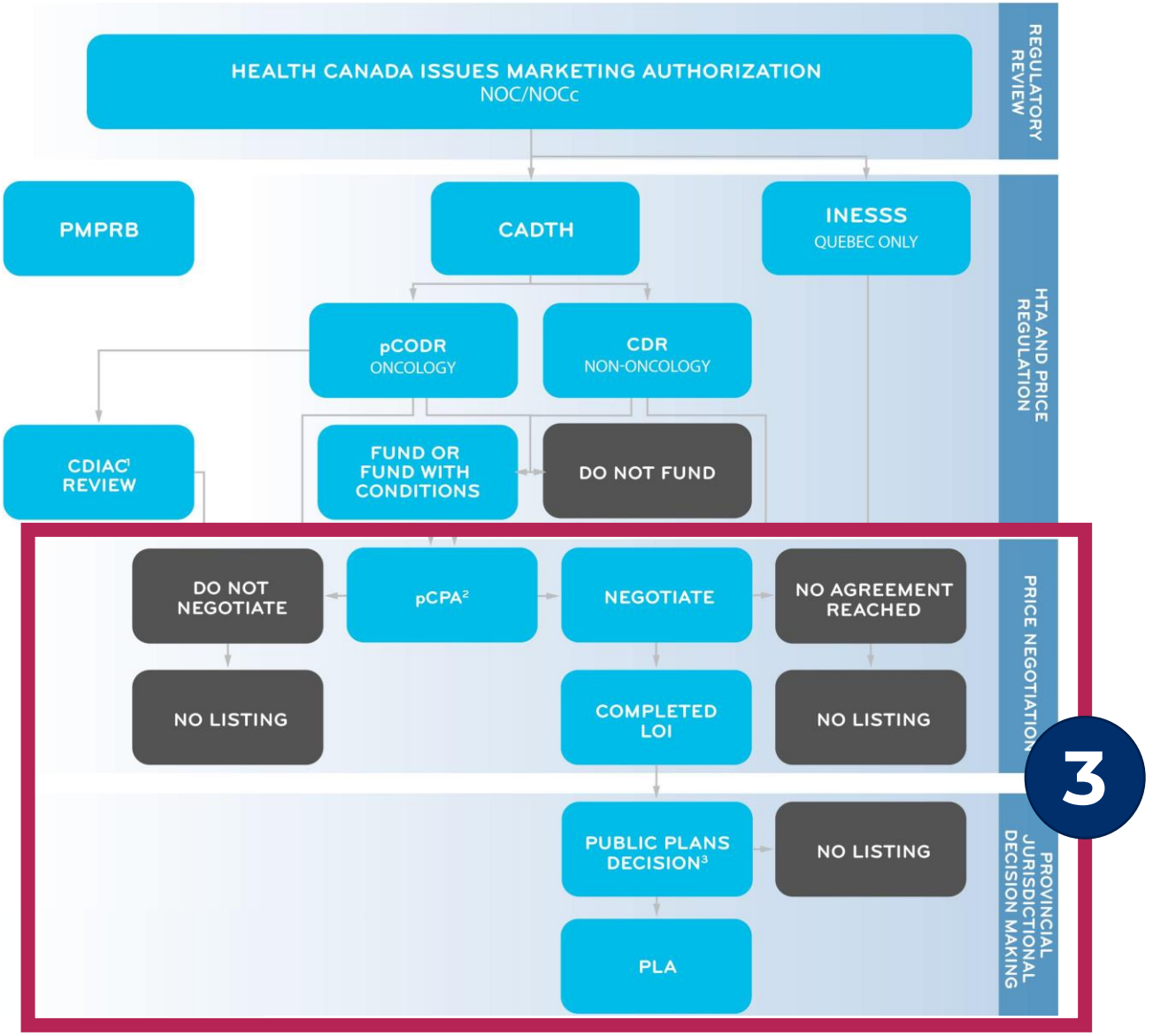
Source: EVALUATION OF DRUGS FOR LISTING PURPOSES – A CHANGE OF APPROACH, https://www.inesss.qc.ca/fileadmin/doc/INESSS/Inscription_medicaments/Processus/Evaluation_of_drugs_a_change_of_approach.pdf
Politique québécoise pour les maladies rares, https://publications.msss.gouv.qc.ca/msss/fichiers/2022/22-916-01W.pdf

SECTION

PUBLIC PAYER DRUG FUNDING

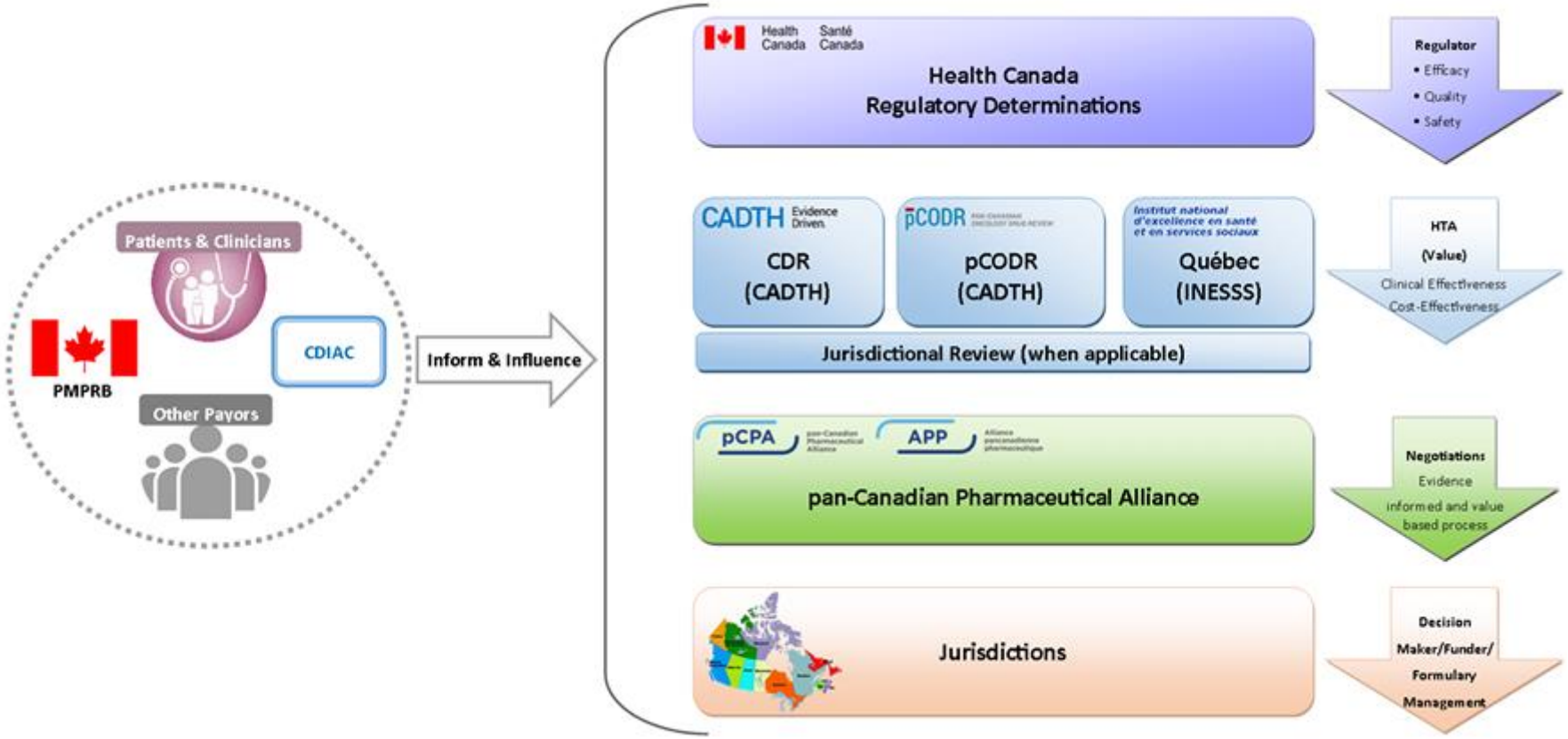
NEGOTIATIONS AND LISTING TROUGH THE PCPA PROCESSS

Drug approval, review, and public funding in Canada is a complex and multi-stakeholder process.



Source: Salek, Sam, et al. "Factors influencing delays in patient access to new medicines in Canada: a retrospective study of reimbursement processes in public drug plans." Frontiers in Pharmacology 10 (2019): 196.

The pan-Canadian Pharmaceutical Alliance (pCPA) is a coalition of all provincial and federal public drug plans in Canada.



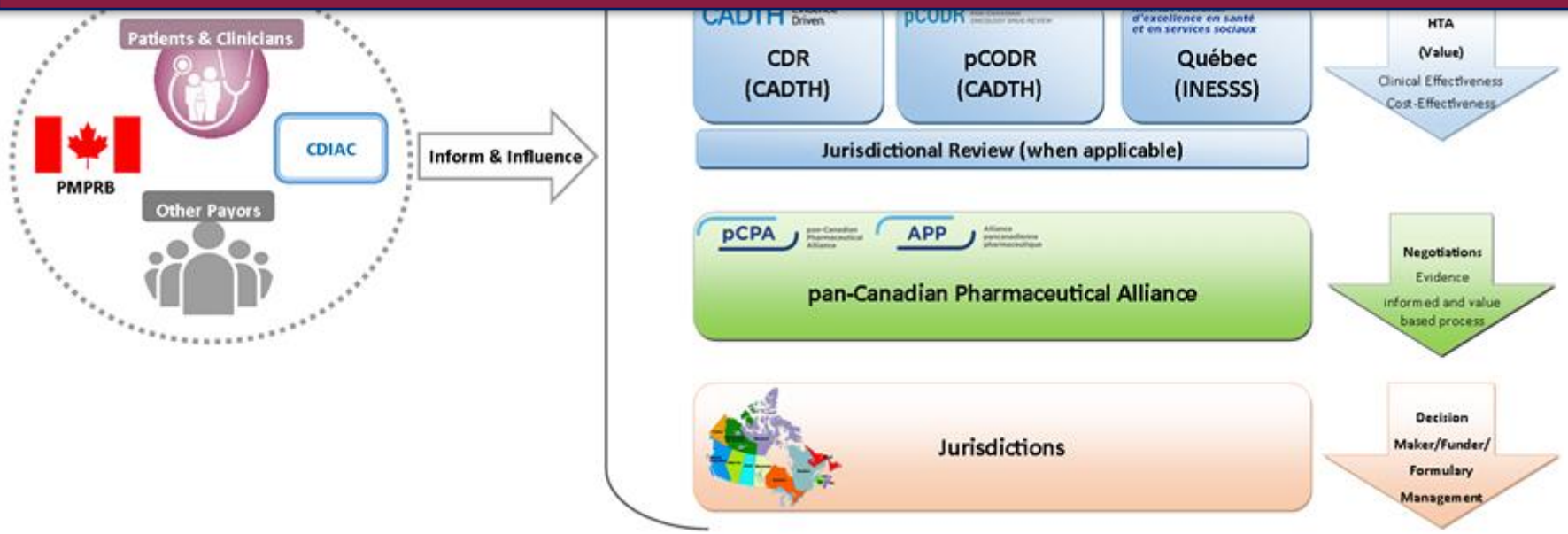
Source: pCPA Brand Process Guidelines, https://www.pcpacanada.ca/sites/default/files/aoda/pCPA_Brand_Process_Guidelines_EN_FINAL-s.pdf

The pan-Canadian Pharmaceutical Alliance (pCPA) is a coalition of

NOTE:

The pCPA is the national body responsible for negotiating the **confidential net price** of the drug, as well as initiation / renewal criteria.

A separate body (the Patented Medicine Prices Review Board, PMPRB) monitors and regulates the publicly available drug list price.



Source: pCPA Brand Process Guidelines, https://www.pcpacanada.ca/sites/default/files/aoda/pCPA_Brand_Process_Guidelines_EN_FINAL-s.pdf

LISTING NEGOTIATIONS ARE COORDINATED BY THE PCPA

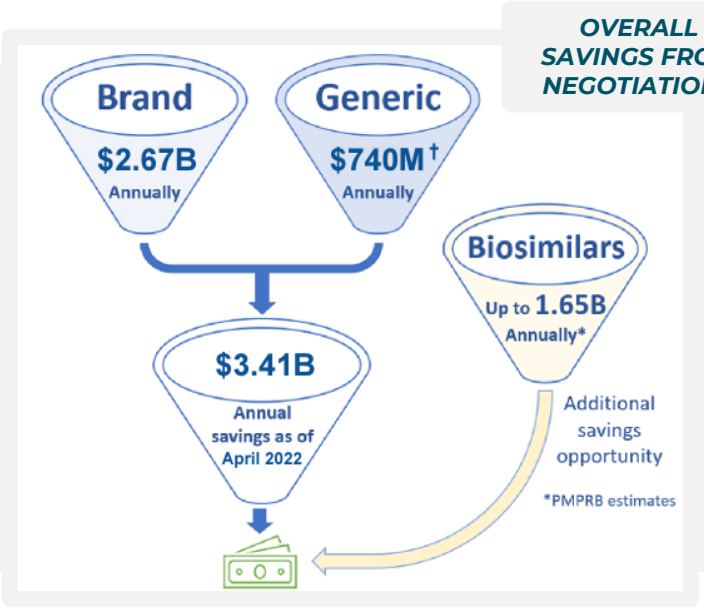
pCPA negotiations follow a four-step process.

1: Initiation	2: Consideration	3: Negotiation	4: Completion
The pCPA evaluates whether new drugs, existing drugs, or line extensions require pCPA consideration	The pCPA gathers information informing whether a drug should enter negotiations	pCPA and the Manufacturer negotiate clinical and financial terms for listing the drug	The negotiation leads to either agreement and a fully executed LOI, or it ends with a close letter
Acknowledgment Letter (LOA)	Engagement Letter (LOE)	Initial Agreement	Letter of Intent (LOI)

pCPA objectives are to:

- Increase access to clinically relevant and cost-effective treatments
- Achieve consistent and lower drug costs
- Improve consistency in funding decisions
- Reduce duplication and optimize resource utilization

OVERALL SAVINGS FROM NEGOTIATIONS



Source: pCPA Dashboard, https://www.pcpacanada.ca/sites/default/files/EN_2022_08_03_pCPA_Dashboard_UPDATE_EO_April_2022_FINAL-s_1503601.pdf

At any given time, the number of drugs being reviewed / negotiated by the pPCA is high.

Not all negotiations are successful.

Status	Total Negotiations	Summary
Active Negotiations	31	Non-oncology: 20 Oncology: 11
Under Consideration for Negotiation	37	Non-oncology: 19 Oncology: 18
Completed Negotiations	544	With Letter of Intent: 469 Without agreement: 75
Negotiations That Were Not Pursued	91	

Source: pCPA Activity Overview, https://www.pcpacanada.ca/activity-overview

LISTING NEGOTIATIONS ARE COORDINATED BY THE PCPA

The process is considered complete once the negotiation has resulted in mutually agreed upon terms and a fully executed Letter of Intent (LOI)

Or, if mutually agreed terms are not reached, the pCPA issues a Close Letter to the Manufacturer, indicating that the negotiation is closed.

!! Even after completion of negotiations and execution of an LOI, it is the responsibility of the individual Jurisdictions and the Manufacturer to transfer the terms into a product listing agreement (PLA) !!

The LOI is not binding.

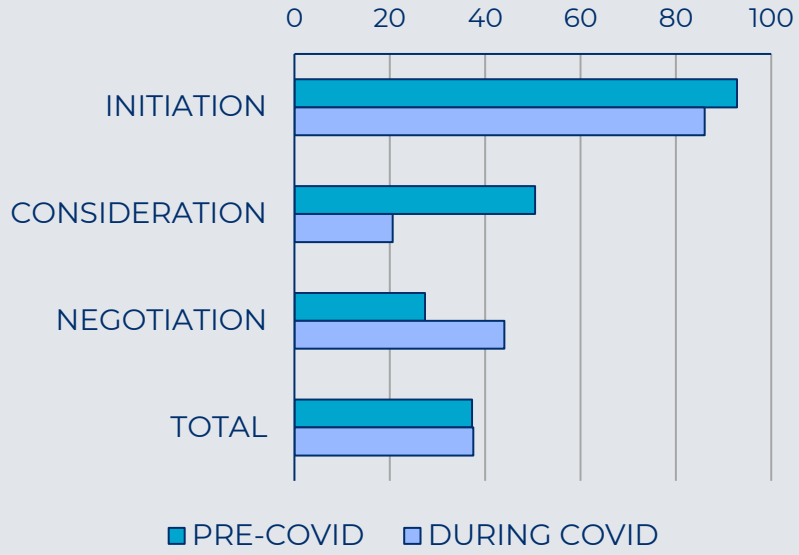
Source: pCPA Brand Process Guidelines, https://www.pcpacanada.ca/sites/default/files/aoda/pCPA_Brand_Process_Guidelines_EN_FINAL-s.pdf

LISTING NEGOTIATIONS ARE COORDINATED BY THE PCPA

The pCPA has target timelines for negotiation processes.

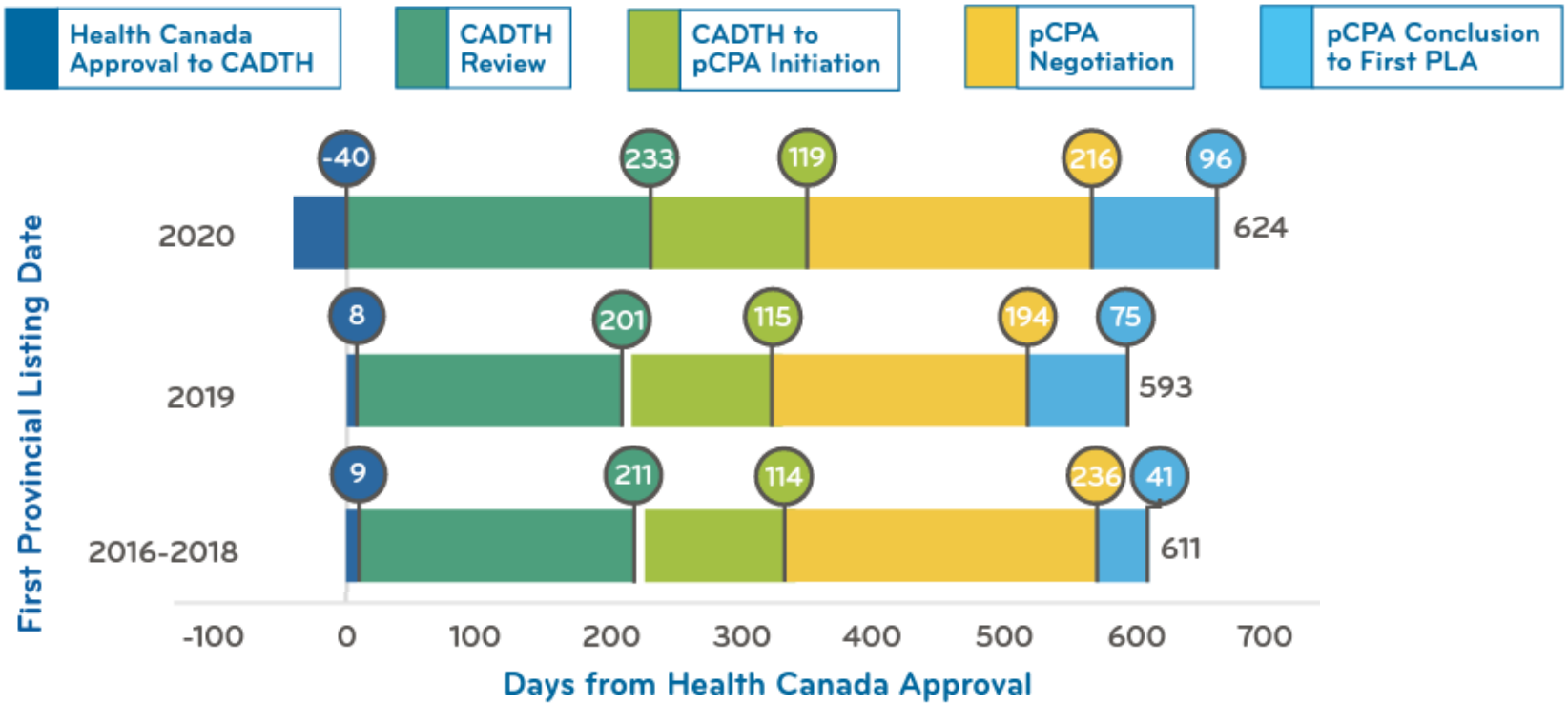
Even if the entire process was on target, the negotiations would take 140 business days (~200 calendar days).

Phase	Associated Deliverable	Target Completion Time
1 - Initiation	Acknowledgment Letter	≤ 10 Business Days from HTA recommendation†
2 - Consideration	Engagement/Close/Hold Letter	≤40 Business Days from HTA recommendation†
3 - Negotiation	Proposals/Counterproposals	≤ 90 Business Days from Engagement Letter
4 - Completion	LOI/Close Letter	



Source: pCPA Brand Process Guidelines, https://www.pcpacanada.ca/sites/default/files/aoda/pCPA_Brand_Process_Guidelines_EN_FINAL-s.pdf
pCPA Dashboard, https://www.pcpacanada.ca/sites/default/files/EN_2022_08_03_pCPA_Dashboard_UPDATE_EO_April_2022_FINAL-s_1503601.pdf

Drugs first listed on Canadian public plans in 2020 were approved by Health Canada almost 21 months before first listing on a provincial formulary. Time to a first provincial PLA continues to increase over time.

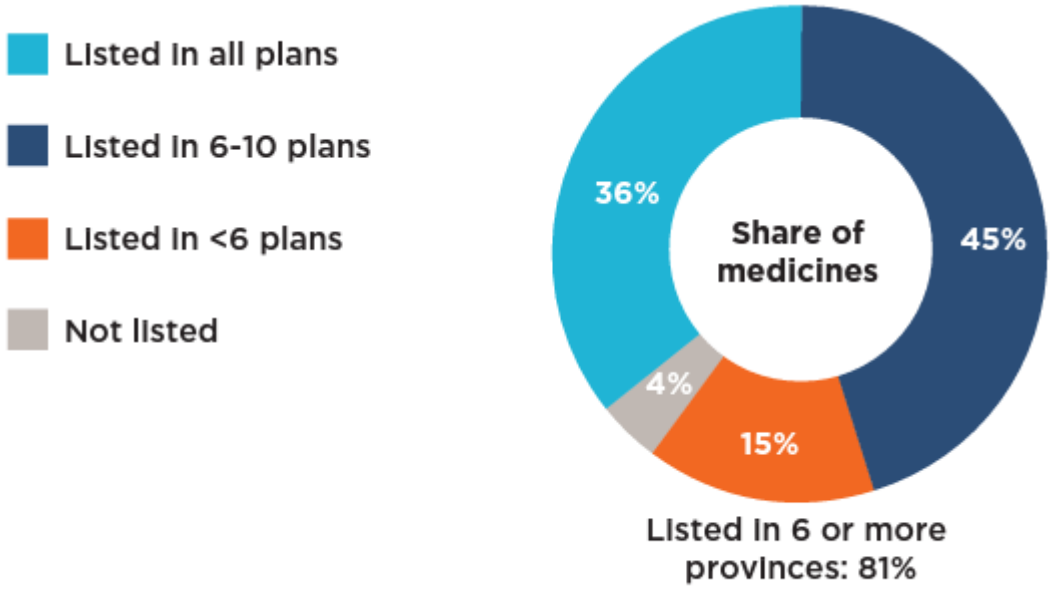


Notes: Excludes Québec listings.

Source: CANADIAN PUBLIC INSURANCE PLANS AND DELAYS IN PATIENT ACCESS TO INNOVATIVE MEDICINES; https://innovativemedicines.ca/wp-content/uploads/2021/12/20210100-PublicDrugReimburse-EN.pdf

However, positive CDR recommendations do not guarantee listing on provincial formularies and not all drugs are listed

Distribution of medicines with positive CDR recommendations by number of public formulary listings (2003-2019)*



*Based on 240 medicines with positive recommendations by CADTH's Common Drug Review, assessed between December 16, 2003, and June 30, 2019. Public drug programs from British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, and Newfoundland and Labrador were included, as well as Yukon and the NIHB.

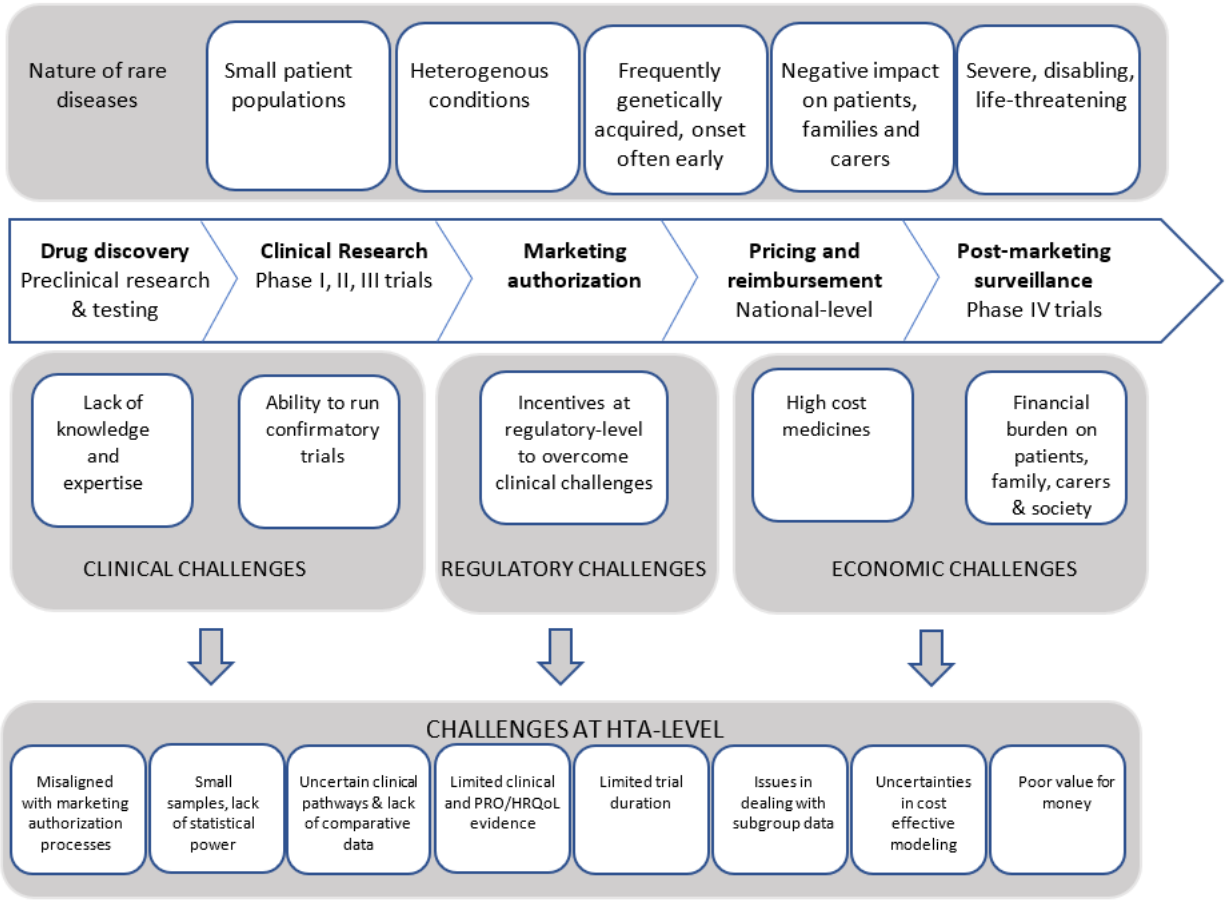
Source: ALIGNMENT AMONG PUBLIC FORMULARIES IN CANADA, PART 3: MEDICINES ASSESSED BY THE COMMON DRUG REVIEW, https://www.canada.ca/en/patented-medicine-prices-review/services/npduis/analytical-studies/formularies-part3-medicines-assessed.html

SECTION

DRUGS FOR RARE DISEASE

ADDITIONAL CONCERNS AND CHALLENGES

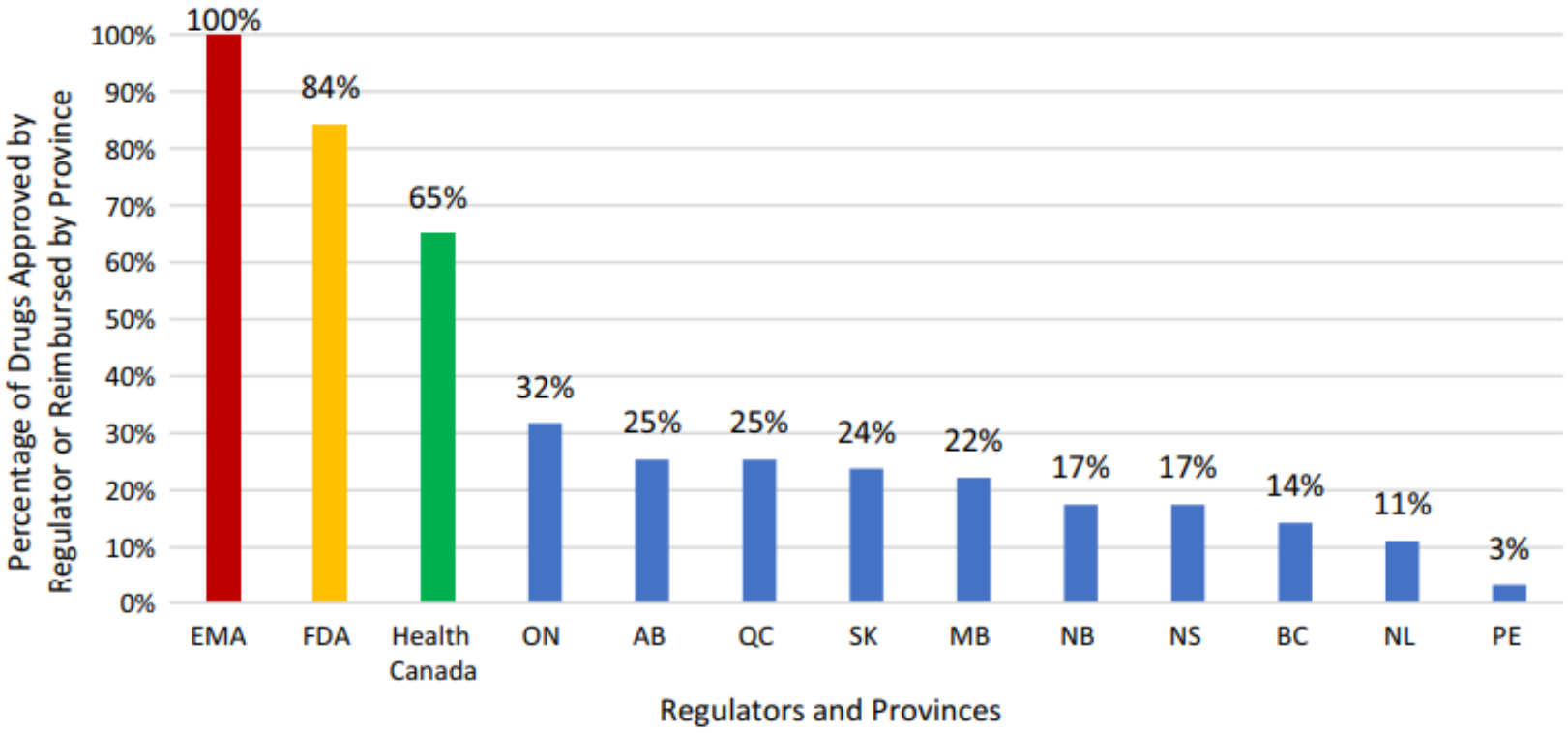
Drugs for rare disease face a number of challenges that make regulatory approval and HTA review challenging.



Source: Nicod, Elena, et al. "HTA programme response to the challenges of dealing with orphan medicinal products: process evaluation in selected European countries." *Health Policy* 123.2 (2019): 140-151.

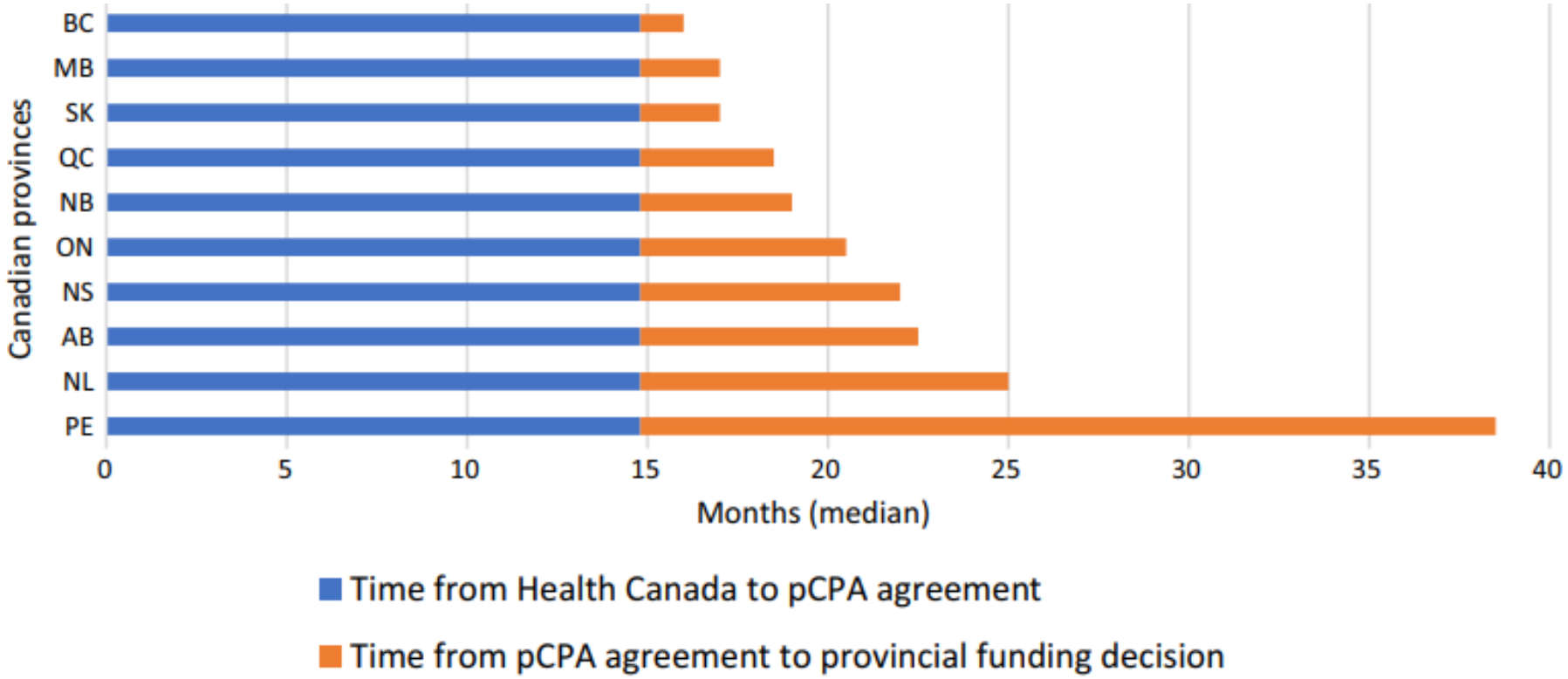
Less than 1/3 of EMA-approved orphan drugs (2015-2020) were publicly funded in Canada.

Ontario had the most public patient access of the provinces funding 20/63 (32%).



Source: Ward, Leanne Marie, et al. "An international comparative analysis of public reimbursement of orphan drugs in Canadian provinces compared to European countries." Orphanet journal of rare diseases 17.1 (2022): 1-14.

Time to provincial funding for DRDs also varies across provinces.



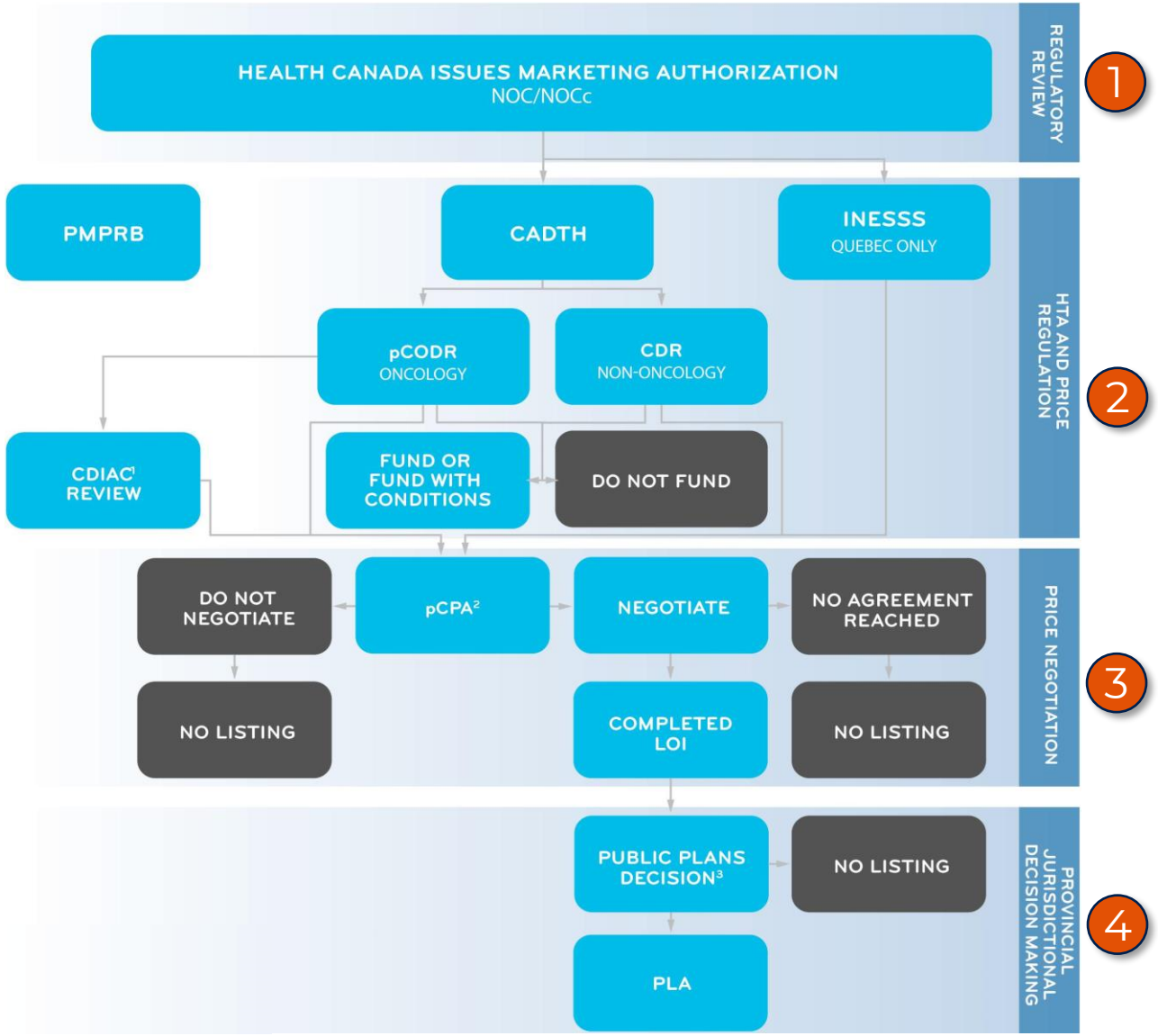
Source: Ward, Leanne Marie, et al. "An international comparative analysis of public reimbursement of orphan drugs in Canadian provinces compared to European countries." Orphanet journal of rare diseases 17.1 (2022): 1-14.

SECTION

Summary

DRUG APPROVAL AND PUBLIC FUNDING IN CANADA: AN OVERVIEW

Drug approval, review, and public funding in Canada is a complex and multi-stakeholder process.



Source: Salek, Sam, et al. "Factors influencing delays in patient access to new medicines in Canada: a retrospective study of reimbursement processes in public drug plans." Frontiers in Pharmacology 10 (2019): 196.

KEY TAKEAWAYS

1. **Drug approval and funding in Canada is disjointed and involves a large number of stakeholders.**
2. **Patient and clinician engagement is a KEY aspect of the HTA process. Ensure your voice is heard!**
3. **Drugs for rare disease face unique challenges, which can lead to further delays in access.**

SECTION

THANK YOU