Memorandum from the Quebec Cancer Coalition

The need for a drug evaluation framework for rare *conditions*

JUNE 8, 2021

To:
The Minister of Health and Social Services; the Ministry of Health and Social Services (MSSS), the National Institute of Excellence in Health and Social Services (INESSS), the Régie de l'assurance-maladie du Québec (RAMQ), the Ministry of the Economy and Innovation (MEI), Treasury Board

Quebec
Cancer Coalition

After more than a decade of lobbying and proposals by several patient groups, including the Regroupement Québécois des Maladies Orphelines (RQMO), the Quebec government is currently developing a policy on rare diseases. The initiative is relevant and appreciated but lacks the opportunity to modernize the assessment of drugs and health technologies to include the notion of rare *conditions*. The stakes are high and are measured in lives saved and cost savings. The development and deployment of a framework for the evaluation of treatments for rare conditions should aim to include a patient population defined by similar epidemiological considerations and not by restrictive nomenclature. This memorandum from the Quebec Cancer Coalition summarizes this issue and our recommendations.

Rare *diseases* and Rare *conditions*

01. A rare *disease* affects **fewer than one in 2,000 people**. This does not mean that the phenomenon is marginal. With thousands of rare diseases, it is estimated that 6% to 8% of the population is affected[1]. Experts anticipate that the number of people with a rare clinical situation is even greater; this number must be added to the number of people suffering from rare diseases under the term 'rare condition.'

02. We define rare *conditions* by the clinical rarity of the prevalence of a specific condition (at the same rate as for rare diseases) that could be targeted by precision treatments. This includes rare diseases, but also mutations of well-known diseases representing special cases, including genetic and molecular mutations.

03. Many common cancers, such as lung, breast, prostate, or colon cancer, have several mutations that may constitute rare conditions. Haematological cancers, some of which are already recognized as rare diseases, may also have mutations that cause rare conditions. Rare cancers, including paediatric cancers, are more likely to have oncogenic mutations. For example, the presence of biomarkers for EGFR, BRAF, NTRAK, RET, ALK, ROS-1, etc., regardless of the location of the cancer, are rare conditions.

04. Personalized medicine, which is based on the identification and therapeutic targeting of rare genetic and molecular mutations, is developing rapidly. The impact on the effectiveness of new treatments as well as on the improvement of patients' quality of life has already been felt for some years.

05. Precision medicine is one of the pillars of the **Quebec Life Sciences Strategy**, but Quebec has not yet adapted its health system to promote and prioritize it. It should be noted that one of the four objectives of this strategy is "to further integrate innovation into the health and social services network (by) :

- the creation of the Office for Innovation in Health and Social Services;
- support for evaluation in real-life care situations;
- and faster access to promising medicines.[2]»

[1] https://www.inesss.qc.ca/fileadmin/doc/INESSS/Rapports/OrganisationsSoins/ETMIS2011_Vol7_No6.pdf
[2] https://www.quebec.ca/gouv/ministere/economie/publications/strategie-quebecoise-des-sciences-de-la-vie-2017-2027/

06. As with rare diseases, it is not always possible to conduct randomized phase III studies to qualify drugs that may treat rare conditions (e.g., because of the small number of eligible participants). Currently, evaluations for treatments allowing access to innovative medicines for people with rare diseases are done on an exception basis. This exceptional treatment is highly valued by patients, their relatives and their representative groups, but the process is not yet standardized, transparent or even fair.

07. Exceptional patient" or "special medical need" processes are the only current gateways to public access, with cumbersome administration that can make access inequitable or difficult. Most of the time, therefore, standard treatment is prescribed, often with less therapeutic benefit, and/or increased risks of toxicity, and/or loss of quality of life. Ineffective treatment also represents a cost to society that should not be overlooked.

Evolving Context for Drug Evaluations in Quebec

08. In 2011, the Quebec government created the National Institute for Excellence in Health and Social Services (INESSS), which was created by merging the *Conseil du médicament* and the *Agence d'évaluation des technologies et des modes d'intervention en santé*. The creation of the INESSS has made it possible to boost innovation in the field of medicines. "The INESSS carries out its mission in accordance with the values of excellence, independence, openness, scientific rigour, transparency, probity and fairness towards those who use health and social services, while taking into account its resources. [3]» Our Coalition particularly appreciates the rigour, openness and transparency of the INESSS, as well as its role as an innovator and scientific leader in drug evaluation. In particular, we applaud the modernized simultaneous approval process for companion diagnostics, among other innovations.

09. Ten years later, Quebec is a leader in Canada in the treatment of rare diseases. Exceptional evaluation methods have been developed in a few very specific situations to offer access to innovative drugs in those situations where the small number of patients makes it impossible to carry out randomized stage III studies, the type of studies recommended by health technology agencies (ATS) such as the INESSS. Since the end of 2018, four drugs for rare diseases[4] have been recommended with certain conditions by the INESSS as exception drugs, with collection of evidence in real-world settings *(RWE)*, and mitigation of economic burden via outcome-based agreements *(OBA)*.

[3] https://www.inesss.qc.ca/a-propos/mission-vision-valeurs.html
[4] Galafold (October 2018); Spinraza (December 2018); Luxturna (November 2020); Zolgensma (December 2020)

10. Pharmaceutical companies are open to partnership and risk-sharing proposals. The innovative drug would thus be made available (through a conditional approval), but would only be formally reimbursed when evidence is demonstrated in the treatment of the person with this very particular rare disease(according to predetermined criteria and health outcomes).

11. The fact that the government is preparing a rare disease policy means that things are moving in the right direction. The initiative is encouraging but seems to be too limited on the evaluation of new treatments. The notion of evaluating treatments for rare *conditions in order* to achieve real progress in the treatment of people with rare diseases must be integrated into the policy work now.

Towards a Framework for Assessing Rare Conditions

12. In the context of the rare disease policy currently being developed, or not, the INESSS should be able to continue to innovate by adopting an "**evaluation framework for the treatment of rare conditions "** by recognizing **clinical rarity** as a trigger, not tumour site or disease type. This policy would aim to systematize the approach to rarity in care situations to offer affected people a straightforward and equitable process for accessing the best available treatment.

13. A single evaluation framework for rare conditions (*including rare diseases*) would serve to provide the flexibility to address unmet patient needs. This framework would allow the INESSS/MSSS to recognize the promise of therapeutic value and propose measures to confirm this and mitigate residual uncertainty (real-world evidence collection, risk-sharing agreements, etc.).

14. The **framework for evaluating treatments for rare conditions** should ensure that:

- That phase II study (of good quality) may be sufficient to allow access to treatment when a randomized phase III study is not quickly and/or mathematically realistic.
- That unmet patient needs are recognized, based on biomarkers or other signs of mutations.
- That conditional approval is possible based on the recognition of these unmet needs.
- That new and innovative processes for collecting evidence in real care settings are accelerated to enable access to treatment, improve knowledge and enable rigorous evaluation.

- That appropriate experts (e.g. in oncology, neurology, genetics, etc.) continue to be actively consulted and involved with the evaluation and determining appropriate outcomes to measure success of treatment in the context of conditional approvals or outcomes-based agreements.
- That a more targeted Quebec approach to risk-sharing with manufacturers of innovative treatments are allowed, based on performance (achievement of predetermined health outcomes), to ultimately allow for formal reimbursement when the treatment is found to be effective.

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15. The establishment of a *framework for the evaluation of treatments for rare diseases and conditions* would be part of a global trend towards risk-sharing arrangements and real-world evidence gathering in specific situations. Rare diseases and conditions are on the rise worldwide due to a combination of clinical, environmental, and social phenomena and, most importantly, due to a better understanding of the genetic and molecular mutations that underlie these conditions. In this sense, pharmacology is evolving towards precision, or personalized, medicine, offering better therapeutic results, with less risk of toxicity, and limiting the costs associated with ineffective therapies.

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16. Patient organizations should be involved in consultations with HTAs on real-world evidence that reflects the experience and health outcomes that have the greatest impact on patients' quality of life, in addition to clinical data. Specifically, *Patient-Reported Outcome Measures* (PROMs) and *Patient-Reported Experience Measures* (PREMs), which are already beginning to be used by patient groups in their submissions to INESSS and CADTH.

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17. The COVID-19 pandemic has been a test for our health system. In some areas, serious shortcomings have been exposed; in others, the need to find alternatives to existing models has revealed a great capacity for innovation. The network and its institutions must continue to meet the challenge of flexibility and agility.

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18. This major paradigm shift requires a strong political will to bring about change at all levels. The MSSS and the MEI must work in a transversal manner to ensure better care for the population while meeting the objectives of the Quebec Life Sciences Strategy and the Treasury Board. Giving the right treatment to the right patient at the right time should not cost more if we avoid using resources and drugs for treatments that are not effective.

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19. Conditional approvals with outcome-based agreements have been deployed in Europe, the UK and Australia for some years now. It is a mechanism that can mitigate risk, reduce costs to the system, and provide the necessary outcomes for the payer, but more importantly for the patient. Most importantly, it places the burden of proof and effectiveness on manufacturers in the context of limited data, while ensuring better access to the population. They also provide important accountability for real-world evidence, while allowing greater flexibility for TSAs, such as the INESSS, to produce more appropriate recommendations based on new evidence.

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20. By adopting a systemic approach to clinical rarity in health care situations with a **framework for evaluating treatments for rare conditions**, Quebec would position itself among the societies that are defining the health care systems of tomorrow by combining scientific excellence with ideals of equity and transparency. This approach would allow us to position ourselves as leaders in personalized medicine, as envisioned in the development of the Quebec Life Sciences Strategy, and to successfully begin implementing value-based healthcare.