EVALUATION OF DRUGS FOR LISTING PURPOSES

A CHANGE OF APPROACH

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**Project team**

**Authors**
Marie-Claude Aubin, Ph. D.
Michelle Boulanger, B. Pharm, M. Sc.
Marie-Ève Brouard, B. A., M. A.
Marie Hotte, B. Pharm., M. Sc.

**Collaborators**
Stéphane P. Ahern, M.D., M. A., FRCPC, Ph. D.
Sylviane Forget, M.D., M. Sc., FRCPC, CAGF
Bernard Keating, B. Th., M. A., Ph. D.
Luc Poirier, B. Pharm., M. Sc.

**Scientific Coordinator**
Anne-Marie Lemieux, M. Sc.

**Director**
Sylvie Bouchard, B. Pharm., D.P.H., M. Sc., MBA

**Publishing**
Renée Latulippe, M. A., scientific coordinator
Jocelyne Guillot, B. A., graphic designer
Patsy Hayes, graphic designer
Mark & Kirsti Wickens, english translation

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The creation of the Institut national d’excellence en santé et en services sociaux (INESSS), in January 2011, led to the consolidation of the work that was then being carried out by two independent bodies in Québec, one of which evaluated drugs for listing purposes (Conseil du médicament), the other, technologies (Agence d’évaluation des technologies et des modes d’intervention en santé). This consolidation of evaluative knowledge was to provide Québec with a high-calibre body that would evaluate new therapies (drugs and technologies) from a scientific, economic, organizational, ethical and societal perspective.

The mandate to evaluate drugs for listing purposes, which had previously been assumed by the Conseil du médicament, was transferred to INESSS. Section 7 of its establishing Act (hereinafter the “Act”) specifies five parameters that INESSS is to examine before making a recommendation to the Minister of Health and Social Services for the purpose of updates to the List of Medications, the cost of which is guaranteed by the Public Prescription Drug Insurance Plan (“public plan”). This plan was set up in 1997 and is meant to be, as stipulated in An Act respecting prescription drug insurance (Québec), universal (a mandatory minimum coverage for all Quebecers), mixed (public and private) and contributory (financial participation of the insured). The purpose of the plan is to provide all Quebecers fair and reasonable access to the drugs required for their health. In light of INESSS’s recommendations, the Minister exercises his responsibility to list or not the drugs for which a manufacturer has made a request and to determine the appropriate terms and conditions. His decisions result in updates of the List of Medications of the public plan, which is published and administered by the Régie de l’assurance maladie du Québec. INESSS also evaluates drugs for listing purposes in the List of Medications – Institutions in accordance with An Act respecting health services and social services.
In 2011, INESSS adopted the methodological framework for evaluating drugs for listing purposes1 that the Conseil du médicament had developed to conduct evaluations. In 2012, INESSS undertook a revision of its framework to adapt to the changing scientific environment and to the extent to which stakeholders were willing to promote innovation, specifically in oncology. This led to the revision of the process for evaluating cancer drugs and to the development of a collaborative model between the Comité de l’évolution des pratiques en oncologie (CEPO), formerly the Ministry of Health and Social Services’ Direction québécoise du cancer and INESSS’s Comité scientifique permanent de l’évaluation des médicaments aux fins d’inscription (CSEMI). INESSS also expanded its recommendation typology so that it could issue listing notices, conditional notices (with clinical monitoring and/or a reduction of economic burden) and notices of refusal for the drugs that it evaluates.

In 2016, INESSS’s Direction du médicament undertook a revision of the methodological framework of evaluation in conjunction with some of its other directorates and members of the CSEMI. A consultation was conducted with external partners from the pharmaceutical industry or patient and caregiver associations. Given the major changes in the pharmaceutical environment in Québec and partners’ expectations, INESSS continued to cogitate. Meanwhile, some of INESSS’s other directorates were working on developing new tools for evaluating innovative therapies, some non-pharmacological, some a combination of drugs and new technologies.

The purpose of this revision is to update the evaluation process in light of recent developments in the evaluation of drugs and new innovative therapies. Among these developments are the evaluation of drugs that have started prior to receiving a Health Canada Notice of Compliance, the increasing role of biologic agents, biosimilars and drugs for rare diseases, personalized medicine, and pharmacogenomics. Furthermore, INESSS wishes to inform its partners and patients, caregivers and citizens of Québec of the update of its evaluative and deliberative processes.

This document constitutes the first stage of a new evaluation framework that is likely to change in the coming years. INESSS has decided to adopt an iterative approach that will continue while strengthening the different components of evaluation and deliberation. Indeed, in collaboration with different assessment agencies and international experts, INESSS wants to integrate new ways of working into its evaluation process, such as the ongoing evaluation of drugs using real world evidence and the introduction of tools that integrate the perspectives of patients, caregivers and citizens to a greater degree and to help ensure fairness in all drug evaluations. Furthermore, INESSS wants to enhance its evaluation approach to make its deliberations regarding each of the parameters stipulated in the Act more systematic and transparent.

INESSS will therefore continue its work, publishing updates and adding new chapters to this document, which it will draft using what it considers the best evaluation practices. There are several objectives to this sequential approach: promoting a reflective approach to its own evaluation mechanisms and their scope, enabling its partners to adapt to the new evaluation practices, contributing to the advancement of knowledge in connection with the work of other assessment agencies here and elsewhere, and encouraging contributions from its partners, including patients, caregivers and, lastly, all Québec citizens. This approach used by INESSS is also in line with the targets defined in the Québec government’s 2017-2027 Québec Life Sciences Strategy.
The pharmaceutical advances of the past few decades have been very significant and have changed the course of a number of diseases by reducing the morbidity and the associated burden, and, in some cases, their mortality rate. More recently, thanks to advances in pharmacogenomics and personalized medicine, new, expensive drugs targeting small populations or rare diseases, such as certain cancers, have emerged.

Furthermore, substantial changes have occurred in the legislative and political environment with regard to the development, evaluation and optimal use of drugs in Québec and Canada. Among these changes are the adoption of the Québec government’s 2017-2027 Life Sciences Strategy and its joining the pan-Canadian Pharmaceutical Alliance (pCPA). This enables the Minister of Health and Social Services to negotiate confidential drug listing agreements and to conduct calls for tenders with manufacturers in conjunction with representatives from the other provinces. Further to societal requests for speedier market access to innovative and promising therapies, Canada’s approval agency (Health Canada) instituted new conditional authorization mechanisms that provide accelerated access, despite a lower level of scientific evidence than this required in the past few decades. Even more recently, an aligned evaluation process between Health Canada and technology assessment agencies, such as the Canadian Agency for Drugs and Technologies in Health (CADTH) and INESSS, was put in place to reduce wait times between the granting of a Notice of Compliance and listing recommendations. Other changes could result from the work currently being done at Health Canada, CADTH and the Patented Medicine Prices Review Board (PMPRB). All of these elements pose new challenges to drug evaluation, which requires changes in how this mandate is carried out.
Given that drugs are playing an increasingly important role in managing patients and consume a major portion of Québec’s health care budget, both at health care facilities and for the public plan, their optimal use is more than ever a major challenge. It is a question of balancing fair and responsible resource allocation and the sustainability of access to publicly funded health care in Québec. Determining the actual value of drugs is therefore essential. Thus, INESSS is pursuing the shared commitment of the government and its bodies to keep the public interest as its top priority and at the centre of all its activities. Enshrined in its establishing Act, the values that it promotes in its work are excellence, independence, openness, scientific rigour, transparency, integrity and fairness.

The objective of this document is to update INESSS’s drug evaluation process. It contains the overall goals of drug evaluations and the basic principles that apply to all drugs evaluated and to the other products evaluated for listing purposes. One of the most important changes is the adoption of a criteria-based structured approach for evaluating drugs, which will lead to a more methodical and rigorous examination of the different parameters specified in the Act. Therefore, INESSS wants to make more explicit and transparent the different criteria taken into account when examining each of the parameters specified in the Act for evaluation purposes. These criteria lead to an assessment of the drug’s value and, in the end, to a final opinion regarding the reasonableness and fairness of listing it. This approach to evaluating drugs is intended to be comprehensive. It takes into account the results obtained using various scientific and methodological approaches (scientific literature, the experience and expertise of health professionals and other experts, and the experiences of patients and their caregivers). Furthermore, adopting such an approach will help better drive and structure the deliberations of the CSEMI, whose composition reflects the different perspectives mentioned in the Act (physicians, pharmacists, methodology and economics specialists, administrators, ethicists and citizens).

As well, note that throughout its evaluation process, INESSS identifies, assesses and manages any potential or apparent conflicts of interest or role, whether commercial, financial, career-related, relational or otherwise and whether they are individual or institutional in scope. To this end, the principles for managing conflicts of interest set out in INESSS’s code of ethics, including the obligation to disclose, apply to all persons, bodies and groups who take part in its drug evaluations.

**Scope of this document**

Although this document primarily concerns the evaluation of innovative drugs and new indications for already-listed drugs, the principles adopted are also used for other drugs evaluated for listing purposes, in which case they are adapted to the particular situation, such as line extension products (new strengths and new dosage forms for already-listed drugs), biosimilars, multisource drugs (generics and natural health products), diagnostic agents, dressings and nutritional formulas.

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2. For the sake of simplifying this text, the term “drug” includes, in this document, nonpharmacological products evaluated and listed in the formularies.
INESSS carries out its drug evaluation mandate on the basis of the five parameters specified in section 7 of its constituent Act:

In exercising the functions described in paragraph 8 of Section 5, the Institute must first assess the therapeutic value of a medication. If this is not established to its satisfaction, the Institute sends a notice to that effect to the Minister.

If the Institute considers that the therapeutic value of a medication has been established, it sends its recommendation to the Minister after assessing:

1. The therapeutic value.
2. The reasonableness of the price charged.
3. The cost-effectiveness ratio of the medication.
4. 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.
5. The advisability of adding the medication to the list with regard to the purpose of the public plan.

INESSS also uses these five evaluation parameters when performing the functions set out in paragraph 9 of Section 5.

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3. Section 2 of An Act respecting prescription drug insurance: The purpose of the basic plan is to ensure that all persons in Québec have reasonable and fair access to the medication required by their state of health.
INESSS wishes to adopt a new, structured evaluation approach that will enable it to explicitly take into account several criteria and integrate them for decision-making purposes. This approach is based on different formal methodologies that are being used increasingly in the field of health.

This approach requires that the parameters to be examined translate into a set of essential criteria that reflect the basis of the decision to be made. These criteria must complement one another and be assessed with the same logic. The best practices in this area require, among other things, that the nature of the decision to be made be clearly defined, that the criteria be explained and justified, that the information and the data sources used to assess each criterion and the uncertainty associated with it be clearly defined, and that the sources and degree of this uncertainty be indicated and analyzed.

For the purpose of making its recommendations, INESSS has developed six criteria that enable it to take into account all the parameters specified in the Act:

1. The identification of the unmet health need in the intended patient population and the determination of the level of this need.
2. The drug’s ability to confer a clinical benefit.
3. The drug’s efficiency.
4. Level of impact of the medical condition and the drug on the health of the general population.
5. The drug’s level of burden on the system’s budget.
6. The system’s organizational ability to offer the drug.

More specifically, the links between these six criteria and the five parameters specified in the Act are as follows:

- Aspect 1: Therapeutic value
- Aspect 2: Reasonableness of the price charged
- Aspect 3: The drug’s cost-effectiveness ratio
- Aspect 4: Impact of adding the medication on the list on the health of the population and on the other components of the health and social services system
The subsequent sections of this document are aimed primarily at supporting these criteria.

Evaluations based on these criteria are carried out using a process that meets the fundamental requirements of a procedural ethics of fairness and that is in line with the values stated by INESSS. The values that matter most to Quebecers, especially those stated in the Canadian and Québec Charters, are the main sources of ethical guidance. Rigorously examining the different parameters specified in the Act requires taking into account scientific and experiential data from different sources, with due consideration given to their quality and robustness, such as:

- **The scientific literature**
- **Expert opinions**
- **The experience of health professionals, patients and their caregivers**

The quality of the data and consultation methods is used to gauge the strength of the assertions made. The data quality assessment is based on the relevance of the information provided in terms of the needs of the evaluation process, taking into account, for example, the study population, the stage of the disease of interest, and the designs of the selected studies and analyses. It also looks at validity regarding the recognized scientific standards, such as those concerning study designs or consultation mechanisms, and at the validity of the results submitted, especially in terms of concordance and uncertainty assessment.
**PARAMETER SPECIFIED IN THE ACT**

**Therapeutic value**

INESSS uses two criteria to determine the therapeutic value of a given drug:

- The identification of the unmet health need in the intended patient population and the determination of the level of this need;
- The drug’s ability to provide a clinical benefit.

**Criterion 1**

The identification of the unmet health need in the intended patient population and the determination of the level of this need

To identify the unmet health need and to determine how important this need is, INESSS relies on data concerning:

- The medical condition’s impact;
- The extent to which the health need is currently being managed.

**The medical condition’s impact**

The natural course of the illness, its symptomatology, and its impact on the patient’s quality of life, functional autonomy and life expectancy are some of the elements considered when assessing its impact on the patient’s daily life.

**The extent to which the health need is currently being managed**

The ability of treatments to prevent a deterioration, to cure, or to improve the medical condition of interest and the patient’s quality of life is used by INESSS to determine the extent to which the need is currently being managed. To this end, it takes into consideration the efficacy, safety, tolerability and impact on quality of life of the treatments available in Québec.

The unmet health need can be of one of several different types. For instance, it can be a question of preventing or relieving symptoms, prolonging life, attenuating the long-term harmful effects of the condition or the adverse effects of the current treatments or of offering an additional treatment option. The need may already be met in part or in full by other treatments, which is a fundamental consideration in its assessment.
Criterion 2

The drug’s ability to provide a clinical benefit

To determine a drug’s ability to provide a clinical benefit, INESSS relies on data on:

- Its efficacy;
- Its safety profile;
- Quality of life; and
- Its therapeutic characteristics.

INESSS also takes into consideration the drug’s therapeutic intent and its role in the therapeutic arsenal available at the time of its evaluation.

A drug’s ability to provide a clinical benefit is determined by evaluating its efficacy against the main, significant manifestations of the medical condition of interest, its safety profile, its other characteristics that can influence adherence to the treatment and its acceptability, and the potential for improving quality of life compared to that of the comparators.

Efficacy

A drug’s efficacy is its ability to prevent or cure a medical condition or to bring about a beneficial change in its signs and symptoms. The efficacy of a drug being examined is evaluated in relation to that of a comparator. Preference is given to efficacy outcome measures aimed at identifying the clinical benefit for the patient, namely, morbidity, mortality and symptom resolution. However, surrogate markers can be used when the correlation between them and the clinical parameters of interest has been established and is well documented.

Safety profile

A drug’s safety profile, including its adverse effects and tolerability, is examined together with that of a comparator. The severity, nature and frequency of the adverse effects and discontinuations due to these effects are taken into consideration. Clinicians’ and patients’ ability to manage the adverse effects is taken into account as well.

Quality of life

A drug’s quality-of-life benefit is its ability to maintain or provide physical, mental or social well-being. The drug’s impact on quality of life (improvement, maintenance or deterioration) as compared to that of a comparator is taken into consideration. The impact is assessed using validated measurement instruments and patients’ perceptions.

Therapeutic characteristics

INESSS takes into consideration the therapeutic characteristics that affect therapeutic adherence and acceptability relative to those of the comparator, such as the route and
frequency of administration and the device used. These characteristics should be supported by the scientific literature, unless there is justification otherwise. Significant drug interactions are taken into account as well when relevant to the evaluation.

**QUALITY OF THE SCIENTIFIC LITERATURE DATA**

INESSS assesses the methodological quality of the studies submitted by the manufacturer and determines the level of evidence, using recognized analytical tools (e.g., the GRADE approach).

For each drug submitted, INESSS expects to receive the best available data for evaluating the product’s efficacy and safety and, therefore, for assessing the risk-benefit balance. INESSS requires at least one relevant randomized controlled clinical trial, published or submitted for publication, to be included with the evaluation request.

In exceptional circumstances, when it is impossible to conduct a randomized controlled trial, other types of studies – with a lower level of evidence – can be submitted, but they have to be accompanied by a justification. The principle is that the quality of the data submitted be proportional to the potential to conduct a study, taking into account, among other things, the prevalence of the disease and compliance with research ethics requirements.

INESSS accepts, on a complementary basis, abstracts and posters pertaining to the main published clinical studies.

As well, in INESSS’s opinion, Health Canada’s determination of bioequivalence or biosimilarity, is confirmation of the therapeutic value of multisource drugs and biosimilars.

**CONSULTATIONS WITH EXPERTS, HEALTH PROFESSIONALS, PATIENTS AND CAREGIVERS**

The information provided by experts permits a better understanding of the disease and its course and is used to document the care trajectories and to critically examine the studies submitted in order to better gauge their clinical significance.

The experiential data reported mainly by health professionals, patients and caregivers contribute to the process of determining therapeutic value and enable INESSS to document the actual clinical experience of the medical condition and the treatments. These data thus provide a picture of the symptoms of the disease or medical condition and the benefits and risks associated with the treatments, and are used to document the expectations or experiences as well as the values and preferences that guide their choices.

The information provided by experts and the experiential data provided by clinicians and patients, with consideration given to their representativeness, are gathered in different ways, such as working groups and within the context of the consultation process for drugs to be evaluated by INESSS. Depending on the case, experiential data can also be obtained by
means of a scientific literature review or another recognized consultation method, such as a survey using standardized questionnaires, focus groups or semi-directed interviews.

**DETERMINING THERAPEUTIC VALUE**

The level of health need is assessed on the basis of the seriousness of the disease, its natural course and the availability of treatments, with consideration given to their benefits and limitations. The health need can vary from nearly nonexistent to very significant.

The ability of a drug to provide a clinical benefit is determined according to the significance of the results in terms of the health gain, safety, quality of life or other therapeutic benefits that it provides. Constituting an additional treatment option may be considered a benefit.

The quality of the data submitted and their degree of uncertainty will influence the assessment of the observed gains. As well, the level of the unmet health need determines the degree of tolerance of the uncertainty associated with the data. All these elements are weighed in order to assess the level of the health need and the drug’s ability to provide the desired clinical benefit.

**RECOMMENDATION CONCERNING THERAPEUTIC VALUE**

INESSSS first determines if the drug has therapeutic value. If it is recognized as having such value:

- It is said to be *incremental* if the drug offers an additional objective benefit in terms of its efficacy, its safety profile, the patient’s quality of life or its therapeutic advantages relative to its comparators. It may be considered low, moderate or high, depending on the significance of the results and on their degree of uncertainty;
- It is said to be *similar* if the drug does not offer any additional benefit relative to its comparators.
PARAMETERS SPECIFIED IN THE ACT

The reasonableness of the price charged and the cost-effectiveness ratio

Determining the reasonableness of the price charged for a drug and the drug’s cost-effectiveness enables INESSS to gauge the amount of resources that would need to be invested to provide access to it and to any treatment with the same therapeutic intent for the desired therapeutic outcomes. This evaluation enables INESSS to assess a drug’s efficiency.

Criterion 3

The drug’s efficiency

To evaluate the efficiency of the drug of interest, INESSS juxtaposes data on:

- The clinical effects (efficacy, safety, quality of life and therapeutic properties); and
- The direct and indirect costs associated with resource utilization.

The drug’s efficiency evaluation leads to an assessment of the anticipated benefits of the drug relative to the cost of treating one person with it. It is based on a pharmacoeconomic analysis performed within the population targeted by the requested indication and in comparison with the therapeutic management that the drug in question could modify it if it were listed.

In the case of incremental therapeutic value, the analysis is usually based on a model that simulates the course of the disease and the clinical impact that the treatments have on it. The relevant costs for managing the disease, based on the perspective chosen (mainly a public health and social services or societal perspective) are taken into consideration as well.

In the case of similar therapeutic value, if the product of interest does not have any differential clinical effects relative to its comparator, the drug’s efficiency evaluation is performed by comparing the costs.

DATA QUALITY

INESSS assesses the quality of the pharmacoeconomic analysis submitted by the manufacturer, in particular, as regards the inputs, modelling and methodology.

At least one analysis must be included, in which the choice of design is based mainly on the type of therapeutic value, that is, incremental (cost-utility and efficiency analysis) or similar (cost-minimization analysis). In certain situations, although it is not preferred because it provides a more subjective assessment, a cost-consequences analysis may be relevant.
Using the best available clinical and economic data, INESSS determines the limitations and makes changes to the manufacturer’s analysis so that it can obtain its own results. In certain situations, to evaluate a drug’s efficiency, INESSS may perform its own pharmacoeconomic analysis.

CONSULTATIONS WITH EXPERTS AND HEALTH PROFESSIONALS

The information provided by experts about the disease and its course, the care trajectory and the studies submitted are also used to better assess the significance of the clinical and economic inputs in the pharmacoeconomic analysis.

For their part, the experiential data reported by health professionals contribute to the drug’s efficiency evaluation by allowing a tangible grasp of the patient’s quality of life as regards the symptoms of the disease and the benefits and risks associated with the treatments, and the use of resources for managing the disease and the effects associated with these treatments.

DRUG’S EFFICIENCY ANALYSIS

The drug’s efficiency is gauged according to the result of the pharmacoeconomic analysis, which can be rated from unfavourable to favourable. The quality of the economic and clinical data used in this analysis and their level of uncertainty will influence this assessment.
PARAMETER SPECIFIED IN THE ACT

Impact that adding the medication on the list will have on the health of the population and on the other components of the health and social services system

The assessment of the impact that listing a drug on the list would have on health is based mainly on the health benefits and risks associated with the drug at the general population, societal or public health level. For instance, the impact on caregivers, on the spread of a disease or on the overall improvement in the health of the general population is one element that may be considered.

The impact of listing the drug on the list on the other components of the health and social services system is assessed mainly by means of budget impact analyses. When applicable, other considerations regarding the organization of health care and social services are taken into account.

INESSS uses three criteria to assess the impact of listing a drug on the health of the general population and on the other components of the health and social services system:

- The level of impact of the medical condition and the drug on the health of the general population;
- The drug’s level of burden on the system’s budget; and
- The system’s organizational ability to offer the drug.

Criterion 4

Level of impact of the medical condition and the drug on the health of the general population

To determine the level of impact of the medical condition and the drug on the health of the general population, INESSS relies on data concerning:

- The number of people affected;
- The medical condition’s burden on the population;
- The anticipated benefits or risks associated with the product for the population.

The number of people affected

The population affected by the medical condition is considered a factual element. It is quantified with Canadian or Québec epidemiological data, such as prevalence and incidence rates. In addition, the demographic changes in this population are examined.
The medical condition’s burden on the general population

In the Canadian or Québec context, from a societal or public health care and social services system perspective, the costs due to a medical condition can be evaluated qualitatively or quantitatively at the general population level.

The anticipated benefits or risks associated with the product for the general population

The positive or negative impact, at the general population level, associated with using a given drug can be assessed using different factors: the fluctuation in the number of people who might resume an active life; changes in the risk of contracting a communicable disease; the impact on caregivers, harm, accidents or vulnerable populations; and the possibility of non-optimal use.

Criterion 5

The drug’s level of burden on the system’s budget

To estimate the budgetary burden associated with the drug for the public portion of the public plan and health care facilities, INESSS relies on data concerning:

- The size of the intended market;
- The products whose use would be affected by the listing;
- The market shares; and
- The budget impact when put in perspective.

Determining the level of burden associated with the drug on the system’s budget leads to an assessment of the level of financial effort required to cover it. This determination is based on a budget impact analysis for the requested indication, which is performed from the perspective of the public portion of the public plan or from a health care facility perspective.

The analysis of the impact on the health care system budget takes into consideration the environment regarding the drug of interest, that is, the size of the intended market, the products that would be replaced and an estimate of the market shares that it would capture during the first few years. In certain situations, INESSS considers the context of real-world utilization and puts into perspective the budget impact associated with the requested indication in relation to the resources that one would have to forgo. Concerning this perspective, it can be done both for drug coverage by health care facilities, which are required to balance their budgets, and for the public portion of the public plan.
The system’s organizational ability to offer the drug

To assess the system’s ability to offer the drug, INESSS relies on data concerning:

- The human, material, physical and other resources; and
- The system’s organization.

**Human, material, physical and other resources**

INESSS assesses the impact of using the drug on the various resources in the health and social services system. It may be the impact on the use of health professionals, the need to acquire, or modify the use of, a material resource, or the need to use physical or any other resources in the health care system, such as [companion tests](https://example.com). In addition, information concerning the creation of patient programs is taken into consideration.

**The system’s organization**

The repercussions of using the drug on the system’s organization are factored into the evaluation. Examples include changes in the way care is delivered, the outpatient-to-inpatient or inpatient-to-outpatient transfer of care, and the accessibility of the drug or care throughout Québec.

**DATA QUALITY**

The assessment of the criterion ‘level of impact of the medical condition and the drug on the health of the general population’ is based on the best available clinical, economic and epidemiological data. The reliability of their source and of their methodology, among other things, is taken into account.

For the purposes of the criterion ‘the drug’s level of burden on the system’s budget’, which is determined from a budget impact analysis, INESSS assesses the quality of the modelling and the reliability of the clinical, economic and epidemiological inputs.

For the purposes of the criterion ‘the system’s ability to offer the drug’, INESSS assesses the quality of organizational data provided.

**CONSULTATIONS WITH EXPERTS, HEALTH PROFESSIONALS, PATIENTS AND CAREGIVERS**

The information provided by experts regarding the epidemiology of the disease, the treatments currently used, and the role of the drug of interest in the therapeutic arsenal enables INESSS to critically examine and validate the different inputs considered in the budget impact analyses. These assessments also enable it to identify and document the considerations regarding public health and the organization of care and services.
Patients’ and their caregivers’ experiences enrich the data on geographical, financial and organizational accessibility, and these experiential data enable INESSS to better assess the impact of the patients’ illness on their caregivers’ lives, both personal and professional.


The level of impact of the medical condition and the drug on the health of the general population is determined on the basis of the number of people with the illness, the level of burden it causes and the level of the anticipated benefits or risks associated with the drug for the population.

As for the drug’s level of budgetary burden on the system, it is assessed on the basis of the significance of the results of the budget impact analysis of listing it, which are evaluated from the perspective of limited resources and the sustainability of public services.

The system’s organizational ability to offer the drug is determined according to the level of impact associated with using the drug on the human, material, physical or other resources and on the system’s organization.

The quality of the data submitted and their underlying level of certainty influence the assessment of these three criteria.
The advisability of adding the medication on the list with regard to the purpose of the public plan

This parameter specified in INESSS’s constituent Act is aimed at integrating all the previous considerations pertaining to the evaluation of a listing request into a succinct assessment, as expressed in the purpose of the public plan, which is “to ensure that all persons in Québec have reasonable and fair access to the medication required by their state of health. To that end, the plan provides for a minimum level of coverage for the cost of pharmaceutical services and medications, and requires a financial participation on the part of persons or families covered by the plan depending, in particular, on their economic situation”.

Determining the advisability of listing a drug in light of the purpose of the public plan is therefore based on all the considerations necessary for assessing fairness and reasonableness. This involves weighing all the assessments of the six criteria examined, namely:

- The identification of the unmet health need in the intended patient population and the determination of the level of this need;
- The drug’s ability to provide a clinical benefit;
- The drug’s efficiency;
- Level of impact of the medical condition and the drug on the health of the general population;
- The drug’s level of burden on the system’s budget;
- The system’s organizational ability to offer the drug.

In addition to these considerations are other elements that may be useful for the deliberations, such as:

- Information on social values and priorities, such as results of citizen and stakeholder consultations, which are published or implemented by INESSS. The quality and representativeness of the consultation mechanisms are assessed according to the relevant standards;
- A targeted review of the literature on the ethical or social issues and concerns, whose quality is assessed according to the relevant methodological and theoretical standards as well;
- The approval and listing decisions made by other authorities;
- The impact on the persons covered by the private portion of the public plan.
Interpreting the uncertainties and the assessments made when evaluating drugs involves implicit and explicit ethical judgments. Indeed, denying or limiting access to a drug, tolerating significant risks in the hope of objectively marginal but subjectively significant benefits, making a decision despite the existing uncertainties, comparing the different disease burdens with one another, and sacrificing the interests of small groups of individuals in the name of the principle of maximizing health benefits for a population are situations that involve ethical judgments, and their results are potentially questionable, according to these same ethics.

It is in this context that determining the advisability of listing a drug in light of the purpose of the public plan requires an overall evaluation that takes into consideration the parameters specified in the Act, the different related criteria and the useful information spelled out in this document. If applicable, this determination will enable INESSS to make explicit the different tensions, the principles for resolving them and the priorities accorded, and to construct an argument that will provide a reasonable resolution for developing a recommendation.
Based on its overall evaluation, INESSS makes a recommendation to the Minister of Health and Social Services concerning the List of Medications for the public plan, the List of Medications - Institutions or both.

The various recommendations that INESSS can make and the situations in which they apply are detailed in the table below. More specifically, INESSS has three categories of recommendations, which are in line with those of other assessment agencies: listing, conditional listing and refusal to list. The wording of the recommendations needed to be simplified, given that drugs can now be listed under an agreement between the Minister and the manufacturer.
### Summary of the recommendations made by INESSS to the Minister of Health and Social Services

<table>
<thead>
<tr>
<th>INESSS recommendation</th>
<th>Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Listing</td>
<td>INESSS makes this recommendation when it considers the assessment of all the evaluation parameters specified in the Act favourable to listing the drug with no restrictions.</td>
</tr>
<tr>
<td><strong>Conditional listing</strong></td>
<td>INESSS makes this recommendation when it considers the assessment of all the evaluation parameters specified in the Act favourable to listing the drug only if certain conditions are met.</td>
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<tr>
<td></td>
<td><strong>POSSIBLE CONDITIONS:</strong></td>
</tr>
<tr>
<td>Exception drug</td>
<td>INESSS suggests this condition when it considers the assessment of all the evaluation parameters specified in the Act favourable to listing of the drug with specific utilization criteria. In such case, it proposes an indication recognized for payment or utilization criteria for the drug.</td>
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<tr>
<td>Monitoring</td>
<td>INESSS suggests this condition in the following situations:</td>
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<td></td>
<td>• When it considers that the drug offers a desired therapeutic value, but that additional clinical data is needed to do a re-evaluation (clinical monitoring);</td>
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<tr>
<td></td>
<td>• When it considers that the drug is associated with a risk of nonoptimal use and that monitoring real world data is necessary in order to do a re-evaluation (monitoring optimal use).</td>
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<tr>
<td>Reduction of the economic burden</td>
<td>INESSS suggests this condition in the following situations:</td>
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<td></td>
<td>• When it considers that the drug’s efficiency is unfavourable (not cost-effective);  or</td>
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<td></td>
<td>• When it is unable to evaluate the drug’s efficiency (efficiency not estimable);  or</td>
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<td></td>
<td>• When it believes that listing the drug would have an unfavourable budgetary impact that could have repercussions on the health care system.</td>
</tr>
<tr>
<td>INESSS recommendation</td>
<td>Applicability</td>
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</table>
| **Refusal to list**   | INESSS makes this recommendation in the following situations:  
  • When it considers that the drug’s therapeutic value has not been demonstrated;  
  • When it considers, in particular, that the level of the patients’ health need is almost nonexistent, that the level of uncertainty regarding the drug’s efficiency is too high and, when applicable, that it is not advisable to negotiate a listing agreement for the drug. |

<table>
<thead>
<tr>
<th>Other recommendations</th>
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<tbody>
<tr>
<td><strong>As part of its work, INESSS may re-evaluate a drug’s listing, be it in the <em>List of Medications</em> for the public plan or in the <em>List of Medications – Institutions</em>. Consequently, it may or may not recommend modifying the drug’s listing. In such case, the following options may apply: modify/do not modify a recognized indication, maintain/delete/transfer the listing or grant/do not grant an exemption from the application of the lowest price method.</strong></td>
</tr>
</tbody>
</table>
Conclusion

This document is a first step in the update of the process INESSS uses to evaluate drugs for listing purposes. This work is being carried out in tandem with that of INESSS’s other divisions in the area of innovative therapies and will continue, given the ongoing scientific, economic and regulatory turbulence.

At the centre of this first exercise, INESSS has set up a structured, criteria-based approach for evaluating drugs for listing purposes. This approach will be adjusted and enhanced through a reflective, multi-criteria process. INESSS and members of the CSEMI want to improve the quality of the approach for analyzing and evaluating drugs in the interest of transparency, fairness and equity. It is important that INESSS be able to make recommendations to the Minister of Health and Social Services where the reasons and considerations, which are made public, are clearly explained and understandable to all the stakeholders. Such communication is essential for highlighting the efforts undertaken to achieve the objective set out in the Act, which is to ensure that all Quebecers have reasonable and fair access to the medication required for their health.

Several initiatives will be launched or continued in the coming months to ultimately strengthen an institutional framework for assessing technologies and intervention modalities for the purposes of public coverage in Québec. This framework will help meet the requirements of the 2017-2027 Québec Life Sciences Strategy and the highest technology assessment standards.

The implementation and optimization of the criteria-based evaluation approach will be continued in order to make the deliberations on all the parameters specified in the Act systematic and to ensure that the different recommendations are consistent. These efforts will serve INESSS’s goals in terms of equity and fairness. Until now, it used an argument-based approach aimed at comparing, on a case-by-case basis, diseases with the same morbidity and mortality burden and at preserving, as much as possible, consistency with previous decisions.
The multi-criteria approach will enable it to identify more clearly the differences between evaluations and to better compare the various situations, using the selected criteria. It will therefore contribute to fairness, which has always been a major concern. INESSS will be working on developing better tools to integrate the information derived from the examination of all the criteria and on clearly defining the arguments and considerations chosen, in order to make a transparent recommendation that can be considered fair, reasonable and equitable to the different decision-making levels and the stakeholders.

One of the discussions to be undertaken will concern the development of new tools for including and interpreting real world evidence when evaluating therapies and during the occasional re-evaluation of actual gains following their coverage.

Also planned is the introduction of tools for further integrating the patient, caregiver and citizen perspectives into the evaluation process. INESSS wishes to enhance its assessment of therapeutic value or added value in light of patients’ and their caregivers’ experiences regarding the disease. The purpose of this is to enrich certain clinical trial data. It is also aimed at better understanding the patients’ experience of the disease, their expectations of the innovative therapy, and their fears. INESSS is keenly aware that these are two different paradigms, one being evidence-based evaluation characteristic of the scientific methodology used in randomized controlled trials, the other an experiential approach used in qualitative research. INESSS also wishes to improve its consideration of citizen deliberation, especially for innovative therapies at the frontiers of tomorrow’s medicine, as regards the impact on the societal representations of health, disease and death, but also on that difficult-to-achieve balance between the individual patient’s interest and collective health needs.
Health Canada has instituted new approval mechanisms that permit faster access to new therapies. INESSS wants to develop better tools for assessing and managing the uncertainties associated with the early evaluation of innovative therapies whose anticipated health value is considered high. The repercussions of faster access to these therapies need to be thoroughly examined. New mechanisms for including these therapies in the public plan will have to be explored so that the financial risks associated with these uncertainties can be shared and the risks, in terms of safety, can be managed responsibly. The Notices of Compliance that Health Canada has been issuing since 1991 are opening the door to these new mechanisms by integrating, as soon as these therapies become accessible, the obligation to reassess the impact, notably by evaluating real world evidence. What’s more, the marketing of products combining pharmacological and nonpharmacological technologies requires a more systematic approach to their introduction.

In a changing scientific and social environment, INESSS believes that it is crucial to propose continual efforts to improve the quality of its evaluative and deliberative processes. In addition to strengthening the collaborations within its walls, INESSS wishes to adopt an open, contributive approach with its partners in order to understand their concerns regarding these new evaluative tools or approaches. Committed to carrying out its mandate and to achieving the goals set out in the 2017-2027 Québec Life Sciences Strategy, INESSS is presenting this update of its approach to evaluating drugs for listing purposes with great enthusiasm and considers that it is a major step forward for patients, caregivers and citizens of Québec.
The websites cited were all consulted on July 25, 2018.


Québec Laws


Loi sur les services de santé et les services sociaux (chapitre S-4.2). Disponible à : http://legisquebec.gouv.qc.ca/fr/showdoc/cs/S-4.2.