Development of a Tool for the Oversight of Innovative Treatments

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Background

- In Quebec, the head of the pharmacy department is responsible for establishing the drug utilization rules of his center.
- Innovative treatment needs increased oversight, but prescribers may not be equipped to provide a complete justification for their request.
- In some situations, the decision is complex because of uncertainties and risks.

Objectives

- To illustrate the complexity associated with innovative, emerging and off-label treatments and to facilitate their oversight

Methodology

- Creation of a multidisciplinary committee with representatives with different expertise.
- Identification of typical situations and issues surrounding the safe use and access to drugs.
- Development of a tool intended for clinicians and decision-makers.
- The tool was tested with several examples of drugs with special considerations, such as innovative, emerging and off-label drugs.
- Iterations to the tool were made when necessary.

Results

Multidisciplinary committee

- The multidisciplinary committee met twice in 2021.
- The committee included representatives from the pharmacy, research and clinical ethics committees, research center, legal affairs office, patients/caregivers' associations, researchers and doctors.
- Multiple difficulties related to drug access were identified depending on the federal, provincial and regulatory legal framework and other uncertainties (e.g. intended indication, available evidence supporting use, benefit/risk balance).

Tool

- The process for creating the tool required approximately 30 versions to account for all considerations.
- The final tool is a figure in which **5 key questions** must be asked. These questions are further divided into **ten independant considerations**, each consists of a risk gradient that is illustrated as a grey scale (Figure 1).

1) What is the intent of the treatment?
2) What is the uncertainty?
3) What is the legal status of the drug?
4) What are the accessibility considerations?
5) Are there other considerations?

- The more a consideration is dark grey, the more risky/uncertain it is and the more oversight is required.
- The extent of this oversight can vary:
  - Some measures are mandated by the legal framework.
  - This oversight comprised three risk management strategies (Figure 2).

Patient-level
Verbal or written consent.
Consent to care, to publication, to research.

Clinician responsability
Clinician/investigator's commitment to follow-up.
Signature of a contract/agreement.

Other stakeholders
Require justification for use.
Advisory recommendation.
Approval or refusal of use.

Example of stakeholders:

Local
Pharmacy department
Pharmacy director
Medical director
Other departments involved
Pharmacology&Therapeutics committee
Professional services department
Institutional suitability Committee
Multidisciplinary Committee
Clinical Ethics Committee
Research Ethics Committee
Legal affairs office
Government
Provincial instances
Health Canada
External
Manufacturer
Sponsors
Foundations
Professional associations

Figure 2. Example of risk management measures

	Considerations	Level of risk/uncertainty						
1° Intent	Treatment	Care (treating a patient, optimizing treatment)	Research (produce generalizable knowledge)					
2° Uncertainty	Indication	Canadian product monograph	Off label (supported by evidence of efficacy and safety adapted to the specific population, monograph from another country, established practice)	Off label (new use, quality of evidence justifying indication)	Investigator brochure (research)	No monograph		
	Formulation	Commercial preparation	Extemporaneous preparation (with established preparation method)	Extemporaneous preparation (without established preparation method)	Veterinary product	Not intended for human use		
3° Status	Canada	DIN	NPN	SAP (serious, conventional treatments ineffective, unsuitable or unavailable)	No canadian status (no status in Canada, not considered a drug)	SPS (care, experimental treatment)	Clinical trial phase IV (without clinical trial application)	Clinical trial phase I, II, III
	RAMQ*	Listed drug		Exception drug	Exception patient		Off list	
	MSSS*	Listed drug		Exception drug	Off list (particular medical necessity)			
	Institution	Listed on local list (with/without particularity, with/without use rules)		Off list	Emerging treatment			
4° Access	Supply	Manufacturer / wholesaler (regular supply)		Manufacturer (special agreement, requirement to create a clinical trial)			Import (drugs in patient's possession, online purchase)	
	Financing	MSSS* (as per list and criteria for use)	RGAM* (RAMQ or private insurance)	Institution (insitution expenses, e.g. outpatient dispensing)	Manufacturer (compassionate access)	Sponsors (research)	Foundations (foundations, community org., socio-financing)	Patient
5° Other	Others actor-specific factors	Clinician (care covered by insurance, expertise)		Clinician (insurability problem, e.g. SAP status or contract with manufacturer, lack of expertise, appearance of conflict of interest,concern ofmedical team)				
		Patient (covered by RGAM, favorable risk/benefit ratio, understanding of options)		Patient (not covoered by insurance, not able to consent, incomplete understanding of options, cannot access treatment due to location, less favorable risk/benefit ratio)				
		Institution (adequate infrastructure, expertise)		Institution (lack of infrastructure, patient base not suited to mission, lack of funding, institutional risk (reputation), inability to ensure continuity of care)				

Figure 1. Tool for the oversight of innovative treatments

***Provincial instances**

Abbreviations: DIN: drug identification number; MSSS: Ministère de la Santé et des Services sociaux (Quebec's Ministry of Health and Social services); NPN: natural product number; SAP: Special Access Program; RAMQ: Régie de l'assurance maladie du Québec (Quebec's health insurance board); RGAM: Régime général d'assurance médicaments (Quebec's prescription drug insurance plan); SPS: Single patient study (clinical trial on a single patient as required by Health Canada)

Example

A clinician wants to prescribe a new drug which is **not available in Canada** to **treat** his patient. The drug is marketed in the US in a **commercial preparation** usable for the patient, but not in the intended indication (**off-label use**). The **patient's insurance will not cover** the medication's cost.

A request to Health Canada's Special Acces Program needs to be submitted to obtain a letter of authorization in order to import the drug. The manufacturer accepts to sell the drug, but a contract will need to be drawn up. The institution accepts to cover these costs. The pharmacy and medical directors ask the clinician to justify the use of the drug (scientific evidence supporting use, efficacy/safety monitoring and follow-up). The patient's written consent will be obtain prior to start of treatment.

Considerations are in bold and risks management measures are underlined

Discussion / Conclusion

- This tool offers guidance when innovative treatments are in grey areas and need proper management.
- It will serve as the basis for a conversation between clinicians and decision makers.
- Our center is currently using it with the new requests for innovative treatment. We are planning a training intended for helping clinicians and the pharmacology and therapeutics committee.
- Sharing this tool enables us to exchange best practices when deciding whether or not to use a drug with special considerations, to ensure that it is used appropriately, safely, consistently and equitably throughout Quebec.

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