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Relevance of the prerequisite of the use of an immunosuppressant drug for the coverage of biologic agents (gastroenterology and dermatology)

English summary

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SUMMARY

Relevance of the prerequisite of the use of an immunosuppressant drug for the coverage of biologic agents (gastroenterology and dermatology)

Introduction

Over the past few years, biologic agents have been included in the therapeutic arsenal for treating chronic inflammatory diseases. To ensure responsible use of these costly drugs, their payment is currently only authorized following the use of conventional treatments (notably immunosuppressants), except in the presence of intolerances or contraindications. However, medical associations in gastroenterology and dermatology report a disconnect between coverage information for biologic agents and best clinical practices. At present, when biologic agents must be used without any prior trials of immunosuppressants, patients can, under certain conditions, receive assistance from biologic drug manufacturers for access through a patient support program. In the treatment of inflammatory bowel diseases, the early use of biologic agents through such support programs appears to be an established and widespread practice for several years.

With the coming into force of section 80.2 of the *Act respecting prescription drug insurance* in April 2021, which prohibits the payment or reimbursement of a medication or supply covered by the Public Prescription Drug Insurance Plan, medical associations shared their concerns regarding access to biologic agents without any prior trials of immunosuppressants with the Ministère de la Santé et des Services sociaux (department of health issues and social services) (MSSS). It bears noting that biologic agents, whether they are reference products or biosimilars, are included in the exceptions provided for under the regulation.

To assess the relevance of the prerequisite of the use of an immunosuppressant for the coverage of biologic agents, the MSSS asked the Institut national d'excellence en santé et en services sociaux (INESSS) to draw on the existing knowledge regarding the role of immunosuppressants and biologic agents in gastroenterology and dermatology.

Methodology

First, coverage information for biologic agents listed on Québec drug formulary (or for which the Minister's decision is pending) was compared with that in other Canadian provinces. Then, a rapid review of the literature was performed to identify CPG (Clinical practice guidelines) recommendations regarding the place of biologic agents and immunosuppressants in the treatment algorithm of Crohn's disease in adults and children, ulcerative colitis in adults and plaque psoriasis in adults. Lastly, experience-based and contextual knowledge was gathered through an invitation to receive feedback on the INESSS' work plan and from a consultation panel including gastroenterologists and dermatologists.

Results

The CPGs selected report a lack of quality studies on the best timing for incorporating biologic agents into a treatment plan. However, according to available data and the importance of several other factors, including the risk of complications, the severity of the illness, the response to previous treatments and the associated costs, learned societies made recommendations regarding various sequences of treatment with biologic agents, both before and after a treatment with immunosuppressants.

For the treatment of inflammatory bowel diseases, most of the CPGs selected comprise recommendations as to the use of biologic agents following a conventional treatment that includes 5-ASA (aminosalicylic acids) and/or corticosteroids and/or immunosuppressants. Numerous CPGs, however, report a paradigm shift towards the use of biologic drugs as the front-line treatment, especially for persons at risk of a poor prognosis, to prevent complications, hospitalization and the need for surgery. Very few clinical trials have compared the efficacy of biologic agents and immunosuppressants, and the ones reported are not representative of current clinical practices with biologic agents. Immunosuppressants are generally recommended to maintain complete remission and could prove an acceptable treatment option once remission is achieved with corticosteroids; however, concerns associated with their safety have been raised, notably regarding the risk of hepatosplenic T-cell lymphoma due to thiopurines, such as azathioprine and mercatopurine.

There are few recommendations in the selected CPGs regarding the role of biologic drugs in the treatment of plaque psoriasis. However, all of the CPGs selected agree in recommending the use of biologic drugs following a treatment with conventional systemic agents, which include immunosuppressants (primarily cyclosporine and methotrexate) and acitretin. One CPG also suggests resorting to the early use of biologic agents in special situations. The differential efficacy of biologic drugs and conventional systemic agents was mainly established through indirect comparisons. A network meta-analysis performed by Cochrane reports that most biologic drugs would be more effective than conventional systemic agents at achieving a decrease of at least 90% on the *Psoriasis Area and Severity Index* (PASI90). In addition, conventional systemic agents have certain safety issues: ongoing treatment with cyclosporine is not recommended beyond one year given the risks of nephrotoxicity, acitretin can cause mucocutaneous effects and methotrexate can induce hepatotoxicity.

Opinions of experts and other stakeholders

For the treatment of inflammatory bowel diseases, despite the lack of quality data on immunosuppressants and biologic agents, the experts consulted believe, based on their clinical experience, that biologic agents offer a superior efficacy and a more favourable safety profile compared to immunosuppressants. Given this, they also consider that requiring a trial with an immunosuppressant before allowing the use of a biologic agent exposes patients to risks, among them toxicity, disease progression and complications. To avoid such risks, clinicians report that the use of biologic agents without the prior use

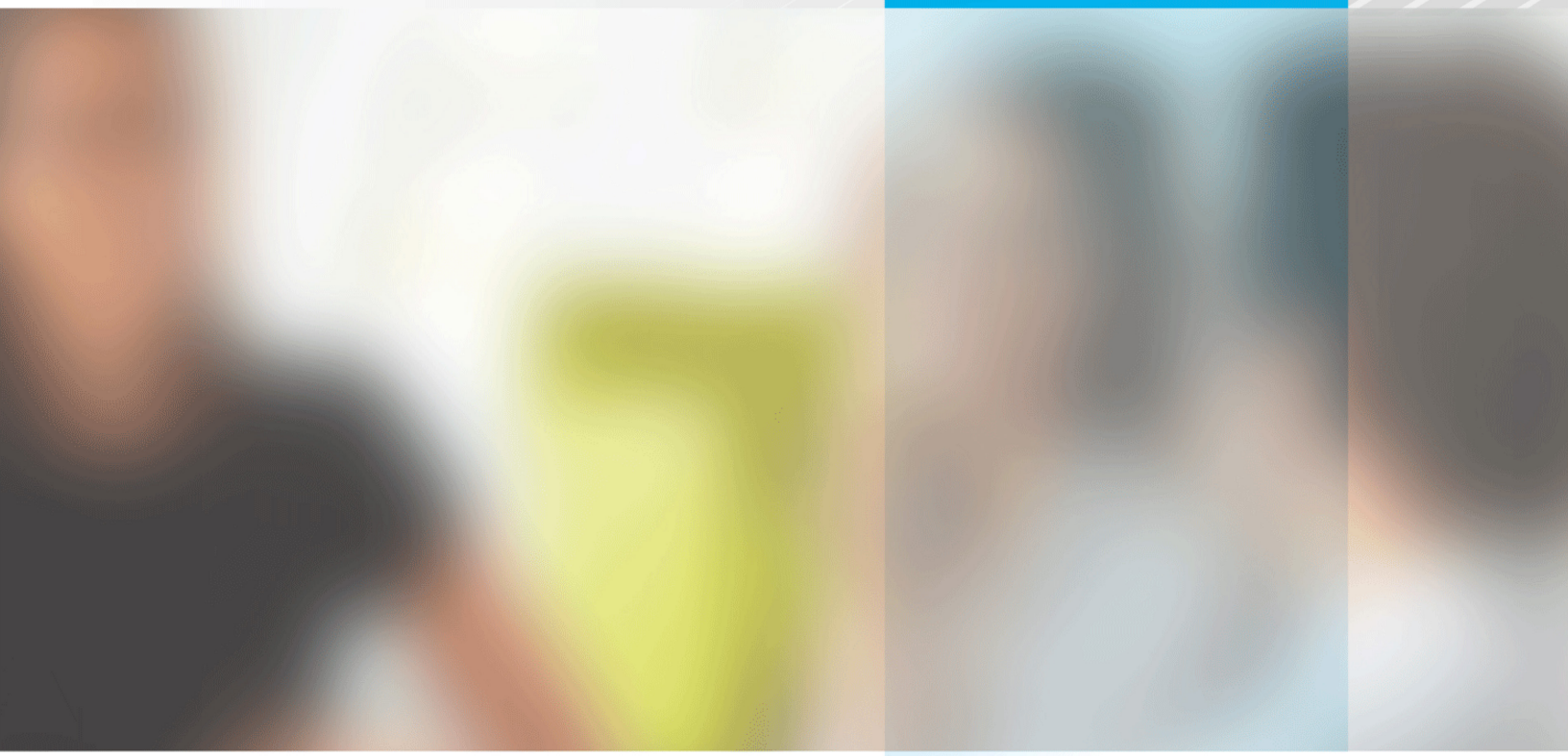
of immunosuppressants through manufacturer-funded patient support programs is a well-established practice in Québec since many years.

Clinicians in the field of dermatology report that the inclusion of preliminary treatments for the coverage of biologic agents in plaque psoriasis could result in patients being inappropriately treated. They mention that among the systemic drugs listed as prerequisite (acitretin, cyclosporin and methotrexate), methotrexate is the preferred agent for treating moderate to severe plaque psoriasis. The clinicians acknowledge that the delays resulting from the trial of at least two traditional systemic agents, as currently required in the coverage information for biologic agents, is not life-threatening for patients. However, they do believe that the treatment should be tailored based on the specific condition of the persons who benefit from it, to reduce psoriatic plaques while limiting the occurrence of adverse effects.

Conclusions

The optimal timing for the introduction of biologics agents versus immunosuppressants in the field of gastroenterology and dermatology has not been assessed in good quality studies. Current research illustrates a discrepancy between actual clinical practices in gastroenterology and the quality evidence-based data available. The clinical experience using biologic drugs to treat inflammatory bowel diseases acquired over the past few years has led gastroenterologists to favour their use without a preliminary treatment with immunosuppressants. Clinicians consider that requiring such a prior treatment with immunosuppressants in the payment indications of biologic drugs for inflammatory bowel diseases should be ceased, mainly because immunosuppressants delay healing and expose patients to risks that include toxicity and non-negligeable complications. And while the circumstances are somewhat different in the field of dermatology, the clinicians consulted also support the removal of this requirement from payment indications of biologic drugs in the case of plaque psoriasis.

Given a lack of data, this work did not evaluate the economic impact of withdrawing the requirement regarding prior treatment with immunosuppressants from the coverage information for biologic agents. This would likely generate a significant increase in costs, but the amounts involved should be compared to the cost of complications and other avoidable consequences. It should also be noted that a large portion of these costs are currently borne by the manufacturers, through patient support programs.



Siège social

2535, boulevard Laurier, 5e étage
Québec (Québec) G1V 4M3
418 643-1339

Bureau de Montréal

2021, avenue Union, 12e étage, bureau 1200
Montréal (Québec) H3A 2S9
514 873-2563
inesss.qc.ca

Institut national d'excellence en santé et en services sociaux
Québec