

Leveling the Field in Canada 2nd Edition

Moving Toward
Reimbursement Equality in
Biologic Therapy for Canadians
with Rheumatoid Arthritis



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1. Introduction

The primary objective of this paper remains the same from the 1st edition released in May, 2010: to provide rationale to allow specialist physicians to prescribe the Health Canada approved biologic response modifier (hereinafter referred to as biologic) most suited for an individual rheumatoid arthritis (RA) patient whenever it is recognized that the particular biologic would provide the best possible outcome for the patient. The secondary objectives are to highlight to government decision-makers in this country the lack of equitable access and patient/physician choice in treating RA with the biologics, as well as to draw attention to the emergence of subsequent entry biologics (SEBs) for the treatment of RA.

Rheumatoid arthritis is the most severe form of progressive autoimmune arthritis and occurs in between 400,000 to 600,000 Canadian adults. RA is a debilitating autoimmune disease that most often affects people in the prime of their lives (20-50 years of age), but can manifest at any age. RA progressively erodes the synovial joints and surrounding tissues and if left untreated, causes irreversible joint damage, chronic pain and losses of function, resulting in profound losses in quality of life (home, social, work) and a decreased life expectancy.¹⁻⁷

Methotrexate (MTX), which is not a biologic, is the anchor for modern management of RA. While many RA patients do respond to methotrexate monotherapy, as many as a third do not (inadequate responders, IR) or have short-term control before regressing back to an active disease state. Furthermore, methotrexate in full, required dosage can, in some patients, be impossible to tolerate because of side effects.

The biologics are therapies that have been engineered to target and block specific disease pathways responsible for the joint inflammation and destruction characteristic of RA.⁸ The biologics have provided tremendous advances in RA management with many patients experiencing complete clinical control of RA and cessation of progressive joint damage, both in early RA or in those who are inadequate responders to traditional disease modifying anti-rheumatic drugs, including methotrexate. Two general sub-classes of the biologics are recognized: the anti-tumor necrosis factor biologics (etanercept, infliximab, adalimumab, golimumab and certolizumab) and the non-tumor necrosis factor inhibitors (anakinra, abatacept, rituximab and tocilizumab).

Biologics are now the standard of care world-wide for the treatment of patients with moderate to severe RA, but no single biologic therapy is effective in all RA patients. While the long-term use of biologics has proven them efficacious and safe, as demonstrated by numerous clinical studies and as well-described in evidence-based guidelines, there are some differences in the adverse event profiles which must be

All biologic response modifiers have proven efficacy in early rheumatoid arthritis and in methotrexate inadequate responders, as monotherapy, or in combination with other disease modifying anti-rheumatic drugs.

balanced against the risk of untreated disease.

Currently, the majority of biologics available for the treatment of RA in Canada are available only on a case-by-case basis in most of the provinces and territories through their public formularies. While some progress has been made over the last two years, as noted in the updated Biologic Therapies Reimbursement Rating Chart, there remain distinct differences as to which biologics can be administered for the treatment of RA and under what circumstances treatment can be provided. More work needs to be done to resolve the unequal patient access to biologics for RA across this country and a lack of choice for patients and their physicians in treating this disease.

Finally, since 2010 the use of Subsequent Entry Biologics has started to emerge within several therapeutic areas (including RA) and is therefore featured more extensively in this 2nd edition. With the approval by Korea on July 20, 2012 of *Remsima*, a SEB of the RA agent *Remicade*, these treatments may figure prominently in the management of this chronic condition in Canada in the years to come. While we welcome the advent of new therapies, the lack of a level playing field in RA remains of paramount concern.

2. Public reimbursement inequities in rheumatoid arthritis treatment with biologics

According to the Oxford Canadian Dictionary, *discrimination* is defined as ‘an act or policy of unfavourable treatment based on prejudice’. Many different groups face discrimination for a wide variety of reasons – on the basis of age, gender, race, sexual orientation, religion, disability status – and these types of discrimination are generally recognized and understood by the public. What is less often acknowledged is that people living with certain diseases frequently face unfair, unequal treatment based on the type of disease they have. Arthritis is one of those diseases, and more specifically there is inequitable access to biologics approved for RA treatment through the various public formularies.

Quite simply, people who are living with rheumatoid arthritis face discrimination on a daily basis.

It occurs on many different levels—from a friend refusing to believe a child can have arthritis, to an employer refusing to modify a workspace, to one level of government refusing to pay for the treatments approved by a different level of government.

The discrimination that people with arthritis are facing, day in and day out, can feel like it comes from every direction. Negative effects of discrimination against people with arthritis range from feelings of loneliness and isolation, to unemployment and poverty, to disability, joint destruction, and even death.

3. Choice of biologics in rheumatoid arthritis treatment and public reimbursement

The use of biologics is deemed appropriate in those patients with RA in whom therapeutic prerequisites have been met and where the rheumatologist and the patient have agreed an approach with a biologic is desirable.

All of the evidence to date generally supports the impression that there is little difference among the biologics in regards to efficacy in RA management, so comparative efficacy should, to date, have little bearing on the therapy chosen.⁸⁻¹⁰ When weighing the decision of which specific biologic to utilize the clinician should engage the patient in discussion regarding differences in access (publicly or privately funded), administration (intravenous, subcutaneous), and safety (adverse events, serious adverse events, infection, malignancies) among this class of medications with specific consideration of the patient's unique clinical profile including disease duration and pertinent comorbidities.

4. Expert input into public reimbursement of biologics in rheumatoid arthritis treatment

The process in British Columbia illustrates how experts can provide valuable and effective input into public reimbursement of biologics for RA. Through the Rheumatic and Autoimmune Diseases Drug Benefit Advisory and Adjudication Committee (RADBAAC), an individual application for a biologic for RA is reviewed by a rheumatologist and a recommendation to BC PharmaCare is made as to whether to provide that medication through public-funding. The RADBAAC also provides advice to the government on difficult compassionate/exceptional cases or new cases, and helps develop criteria. Although their work is strictly advisory in nature, their adjudications have been consistently followed by BC PharmaCare. Additionally, as part of the enhanced drug review process through BC Pharmaceutical Services Division, there is now a formal mechanism for RA patients, caregivers, patient groups and physicians to provide input into the review of new RA biologics. This makes BC the leader in Canada in comprehensive stakeholder input.

5. Efficacy of the biologic agents for the treatment of rheumatoid arthritis

There are few randomized, head-to-head trials comparing any of the biologic therapies to one another; thus, no definitive rankings of the agents based on efficacy or safety are

possible. Further, sophisticated statistical analyses and systematic reviews have concluded that there are no clear differences amongst the currently used biologics in terms of efficacy.⁸⁻¹³

The efficacy and safety of specific biologics are generally investigated in one of three patient groups: those with early RA naïve to MTX, those who are methotrexate inadequate responders, and those who are inadequate responders to anti-tumor-necrosis factor biologics. Clinical efficacy is typically monitored by the use of assessment scales (eg. American College of Rheumatology scales or the Disease Activity Score) and by assessment of damage by using X-ray (eg. Sharp's score). The efficacy measures (i.e. American College of Rheumatology 20, 50, and 70 responses at six months) are essentially similar among the biologics in both early RA patients naïve to methotrexate (70%, 60% and 45%, respectively) and in those who have responded inadequately to methotrexate (methotrexate inadequate responders) (60%, 40% and 20%, respectively).^{11, 14-39}

a. Efficacy of the biologic agents for the treatment of early rheumatoid arthritis

The effective treatment of RA as early as possible after positive diagnosis is critical to preserve joint integrity since it is documented that joint damage begins within six weeks of RA initiation. The biologics have exhibited significant clinical benefit in the treatment of early RA (i.e. methotrexate naïve patients) and, where assessed, the use of a biologic therapy together with methotrexate has been better than the biologic or methotrexate alone, with one exception.^{11, 14-18, 21, 37, 38, 41-44} These findings demonstrate the potential for the use of biologics and methotrexate early in the disease progression to maintain function and avoid disability.

For the preservation of joint health, treatment for RA should be initiated as close to diagnosis as possible

b. Efficacy of the biologic agents for the treatment of methotrexate inadequate responders patients

While methotrexate is undeniably a key component of the armamentarium to treat RA, there are a large proportion of patients who have an inadequate response to methotrexate alone or in combination with other disease modifying anti-rheumatic drugs. In those who have responded inadequately to methotrexate, anti-tumor necrosis factor biologics have been demonstrated to be significantly more efficacious in improving the clinical signs and symptoms of RA than continuing methotrexate alone.¹⁹⁻²² The durability of anti-tumor necrosis factor biologic response is good in such patients, although some national registries suggest there may be differences among the different medications. Follow-up in open-label extensions has, with some medications, been up to ten years with no new safety concerns becoming evident.

Successful treatment of methotrexate inadequate responder patients has also been

reported with non-tumor necrosis factor inhibitor biologics.^{28-32, 44-46} Similar to what is observed in early RA, in the majority of trials with biologic treatment a better response is attained with the combination of methotrexate and the biologic as compared to either alone.

c. Efficacy of the biologic agents for the treatment of biologic inadequate responder patients

While most patients respond to the first biologic agent, there are still many others that do not obtain a satisfactory response with their first biologic (commonly a tumor-necrosis factor inhibitor). Sometimes loss of efficacy may reflect the development of antibodies to the agent used. All of the available non-tumor necrosis factor inhibitor biologics have proven efficacy in the treatment of those patients responding inadequately to tumor necrosis factor inhibitors.^{33, 34, 36, 37, 40, 47, 48} Thus, the failure of one biologic should not be regarded as a loss of effect for the class as other biologics, with different mechanisms of action, often elicit a positive clinical response.

d. Sequential use and combined use of biologic therapies

There is no definite proof (i.e. randomized control trial data) that supports the switching of one anti-tumor necrosis factor biologic to another in the case of a failure to respond to the first, whether primary or secondary. There is, nevertheless, a large amount of clinical registry data suggesting that this type of switching may be effective and it is supported by one recently published clinical trial (although there may be some reduced adherence and effectiveness with the second biologic agent).^{49, 50} Thus, clinical experience has proved this to be a feasible alternative.

There are no increased concerns of adverse events with sequential use of biologics

There have been no increased risks associated with sequential use of different biologics, whether of the same class or a different one. Thus anti-tumor necrosis factor biologics can safely follow rituximab or abatacept and vice-versa. Several attempts at combined use of biologics have been associated with an increased safety risk and this approach should be avoided.^{51, 57, 59}

e. Damage to joints over time as assessed by X-ray

The slowing or arrest of X-ray damage is one of the important benchmarks for RA therapies, as preservation of joint structure has been demonstrated to significantly decrease the chances of permanent disability. Treatment with biologics has demonstrated a cessation or slowing of radiographic damage after therapy for as long as five years in the majority of treated patients.^{11, 12, 14-18, 22, 25, 27, 29, 31, 32, 34, 35, 39-42, 45, 58, 60, 61-62} X-rays over time prove that biologics are the most efficacious therapy for the treatment for patients with RA.

X-rays over time prove that biologics are the most efficacious therapy for the treatment for patients with RA and because of this have become the global standard of care for progressive RA.

6. Biologic agents and adverse events

When considering a specific biologic for a specific patient a clinician must weigh the biologic's specific benefit with the perceived risk. These infrequent adverse events need to also be balanced with the risk of poorly treated disease and with that of other therapies such as corticosteroids. With the anti-tumor necrosis factor biologics, there are data suggesting increased adverse event incidence as compared with methotrexate monotherapy.⁵²⁻⁵⁸ Thus, while infections may be increased, particularly with higher doses, some anti-tumor necrosis factor biologics are less likely than others to be associated with “opportunistic” infections (i.e. tuberculosis, listeria, fungi). To date, registry data do not support an increased incidence of neoplasia, including lymphoma, except for a small increase in the risk of non-melanoma skin cancers, which are considered an acceptable risk. Longer follow-up in registries and open-label extensions have not shown safety concerns with tumor-necrosis factor inhibitors to increase with time, but rather the reverse.

With respect to the non-tumor necrosis factor inhibitors, there has been no evidence to suggest that the use of anti-tumor necrosis factor biologics prior to or following other non-tumor necrosis factor inhibitors (i.e. abatacept, rituximab, tocilizumab) affects safety and in fact the reverse is true. A biologic with a different mechanism of action can immediately follow anti-tumor necrosis factor biologics³⁶ or after some time has elapsed without undue concerns for safety.

It is clear that the risk of infection is increased with the concomitant use of corticosteroids; one aim in treating patients with RA is to discontinue prednisone or use the lowest dose possible.

7. Subsequent Entry Biologics

Biologics are very complex molecules. They are made with the aid of DNA recombination technology and are secreted by cells, bacteria or plants, which have incorporated the appropriate genes. The drugs are then harvested from the secretions. Sometimes a “second-generation” biologic is made that is structurally different from the original molecule and these are intended to improve performance or perhaps decrease immunogenicity, while preserving the mechanism of action. These second-generation products are not usually considered to be “follow on” products or biosimilars. Biosimilars, or as they are known in Canada, subsequent entry biologics (SEBs), are intended to be sufficiently similar to the reference product that there is no clinically meaningful difference between them in terms of safety, purity and efficacy.

Therapeutic substitution is the interchange of a less costly drug in place of another treatment, based on the premise that the cheaper version has the same therapeutic effect. The generic forms of a reference drug are usually marketed after the patent of a branded agent has expired. A generic drug contains an active component, normally a

small molecule, which is qualitatively and quantitatively identical to the reference drug, although the excipients may differ. Marketing the generic form requires only an abridged procedure as it is not a new chemical in its entity. A SEB does not need to be identical to the original biologic, but what must be an exact copy, is the protein's amino acid sequence. What is expected is that the SEB products will produce the same clinical result in any given patient as the reference drug.

The question that is critical to address is when is a copy good enough to be treated as the real thing, especially with the patents of several top-selling biologic agents in rheumatology expected to expire in the next few years

Clinical trials of SEBs are ongoing in Canada at this time and some of the concerns raised include:

- Will the drug be as effective as the reference drug?
- Will it be as safe as the reference drug, both in the short and long term?
- Will it be as well tolerated as the reference drug? Will the rates of infusion and/or injection site reactions be similar?
- If a SEB is substituted for a prescribed drug, will this have any adverse impact?
- How will the pricing of RA SEB products affect the overall price of the RA biologic class?
- Where will the therapy be administered and will they require similar co-medications as the reference drug?

a. Manufacturing

It is as important for SEBs as for the reference drug that there be development of a manufacturing process that consistently produces the drug substance within the accepted, normal batch to batch variation of the product with respect to the structural features that are most important for the SEB's function. SEBs are required to be "highly similar to the reference product, notwithstanding minor differences in clinically inactive components" and exhibit "no clinically meaningful differences between the biologic product and the reference product in terms of the safety, purity and potency of the product".⁶³⁻⁶⁷

b. Extended indications

This issue remains controversial i.e. whether, if a SEB has shown equivalence to a reference drug in patients with RA, the equivalence still needs to be shown for other diseases for which the reference drug is approved. This question does need to be addressed in initial regulations and in the early stages presumably cannot be routine, as it will require data to determine. But once the area is more advanced, such extended indications could become routine.

c. Immunogenicity

A considerable problem for establishing an abbreviated regulatory pathway is the potential immunogenicity of the drug. For endogenous proteins concerns of immunogenicity are heightened. One example of this is erythropoietin, where immunogenicity has had significant consequences with the development of pure red cell aplasia in a small number of patients. It may well have been a change in the formulation of recombinant human erythropoietin i.e. a change in the protein stabilizer from albumin to polysorbate that led to the development of antibodies, which cross reacted with endogenous erythropoietin.⁶⁸ However, for non-endogenous proteins, concern will generally focus on immunogenicity-related adverse events and on immunogenicity that alters in a meaningful way the pharmacodynamics or pharmacokinetics of a SEB. The corollary to this is that SEBs should have their own specific name such as “infliximab-celltrion” rather than simply “infliximab”.

d. Regulatory framework

The regulatory framework for SEBs varies from country to country.⁶³⁻⁶⁷ Many have established SEB pathways or at least draft guidelines. The first was provided by EMA in 2005 and provided a framework for others to build on. Some drugs have been rejected.⁶⁷

The assessment of similarity with the reference drug is performed throughout the development of the product and will include physicochemical properties, biological activity, immunochemical properties, process and product-related impurities and stability. The pre-clinical studies should be conducted with the final formulation of the SEB intended for clinical use. Demonstration of pharmacokinetic similarity between the SEB and the reference drug is an essential component of this program.⁶⁹ Equally, pharmacodynamic assessments are chosen based on their ability to predict clinical outcomes. Ultimately, similar efficacy between the SEB and the reference drug will generally need to be demonstrated in adequate randomized and controlled trials. Clearly, however, no placebo component will be required in those studies.

Health Canada has developed guidance and clarifications on SEBs, which could have even broader implications⁶⁸. According to Health Canada:

- SEBs are not ‘generic biologics’.
- Marketing approval for a SEB is “not a declaration of pharmaceutical or therapeutic equivalence to the innovator drug”.
- Each approved SEB “is considered to be a new (‘stand-alone’) product with all of the associated regulatory requirements”.
- “Comparative clinical trials are critically important to demonstrate the similarity in efficacy and safety profiles” between the SEB and the innovator drug. This means that they have to be tested in humans, and that the testing has to be robust enough to detect differences.
- For generic drugs, pharmacists are often required to ensure that the cheapest version of the chemical drug is dispensed, even if the physician writes a prescription for the

brand version of a drug. This substitution reflects interchangeability. For biologics, Health Canada does not support interchangeability and substitution (as it does for most generic, small molecule drugs), and recommends for prescribing decisions that “physicians make well-informed decisions regarding therapeutic interchange”. To date, only one drug, the recombinant human growth hormone Omnitrope, has been approved by Health Canada as a SEB. Most provincial health care systems and health care professionals are now treating Omnitrope as one new option in an established class of therapies. Yet few provinces have announced how SEBs will be reviewed and reimbursed. BC PharmaCare has stated that SEBs are required to complete a review via the Common Drug Review prior to a review. However, BC PharmaCare has not indicated how robust the clinical trial program of a SEB need be, nor whether these products will be preferentially reimbursed over other RA biologics. Alberta is the only province that specifically excludes SEBs from being considered as interchangeable.

8. Challenge and Recommendations

THE CHALLENGE – Delivering the most effective rheumatoid arthritis treatment to patients in Canada

a. **Public reimbursement inequities in rheumatoid arthritis treatment with biologics**

- Not all biologics approved for RA treatment are listed on all public formularies. This inequity must be corrected.
- For those biologics that are listed on a particular public formulary, there are often unreasonable restrictions that prevent RA patients from receiving the most effective treatment.

Recommendation: That if there is evidence of a fair response, but one not quite meeting the criteria set by the clinical outcome measures, an extension for re-assessment of response at six months be permitted.

b. **Choice of biologics in rheumatoid arthritis treatment and public reimbursement**

- To provide the most effective treatment, the treating physician, in discussion with the RA patient, must be permitted the choice to prescribe the most appropriate biologic for that individual.

- For those who respond, this results in a return to a “full life” for that person living with RA.

Research supports public formulary policy that allows for the specialist physician to prescribe the “right biologic to the right person at the right time”.

Recommendation: That the choice of biologics should be a shared decision between a physician and patient based on the patient’s specific disease characteristics, preferences and with reflection of his/her co-morbidities and specific risks.

Recommendation: That if a patient has been deemed initially eligible for a biologic, there should be a seamless process when switching to a second or third biologic (if needed) without the necessity of repeating the initial formal application and clinical pro forma.

c. **Expert input into public reimbursement of biologics in rheumatoid arthritis treatment**

- Specialist physicians can provide the appropriate prerequisites for the use of biologics in rheumatoid arthritis, including the development of specific criteria for each medication and within the case-by-case request process.
- An open communication process must be developed to ensure that comprehensive information is available to public formulary decision-makers.
- This results in the best quality of patient care, delivered in a cost-effective manner.

Recommendation: That the provincial and territorial governments seek advice from rheumatologists through a formal advisory framework in determining indication prerequisites.

Recommendation: That some form of appeal mechanism be set up that is satisfactory to patients, physicians, and government to review both approval applications for general approval of a specific drug as well as the needs of specific patients where required.

THE CHALLENGE – Properly utilizing subsequent entry biologics for the treatment of rheumatoid arthritis patients in Canada

d. **SEBs must have an acceptable safety and efficacy profile**

- Significant clinical trial data using accepted outcomes should be required to demonstrate a satisfactory safety profile for each SEB product.
- At this point a SEB manufacturer should be required to provide the same information on their product’s safety and efficacy as the brand name product to which it claims similarity for each specific diagnostic indication.

Recommendation: That there be a national approved brand name biologic to which the SEB in question can be compared for similarity.

e. **SEBs should not be deemed interchangeable with each other, nor with brand name biologics**

- Given the complexity of manufacturing processes of biologic products and the safety concerns highlighted by SEB non-approvals and rejections by the EU, SEB products cannot be declared “interchangeable” with brand name biologics.
- While Health Canada has clearly stated that SEBs are to be considered “similar” to brand name biologics, provincial drug plans have yet to formulate the same policy.

Recommendation: That physicians and patients should remain free to select the most appropriate biological therapy based on the patients’ needs and its history of safe use and clinical response.

Recommendation: That decisions to substitute one similar product with another should only be made at a physician’s discretion.

f. **Each biologic must have a unique product name**

- Given the fact that SEB products are not always identical to innovator products and could have significantly different clinical outcomes for patients, physicians and other

allied health professionals must be able to readily distinguish SEBs on the basis of their names.

- A unique name will assist in the accurate prescribing and dispensing of SEBs and supports governmental efforts to closely monitor adverse events.
- Without distinct names, patients, physicians and pharmacists could become confused, leading to inadvertent product substitution.

Recommendation: That each SEB product has unique and distinguishable name, as well as a distinct name under the International Nonproprietary Names (INN) Program of the World Health Organization.

g. Cost must not override safety and efficacy

- The cost of producing SEBs is clearly less than that of the brand name biologic to which it is similar.
- Assuring patient choice may be problematic for patients who rely on publicly funded biologics, because prescribing physicians may be encouraged or compelled to prescribe the less expensive SEB, thereby potentially compromising patient choice, outcomes and safety.

Recommendation: That SEBs not be given preferential listing on provincial formularies if it is at the expense of patient safety, proven product efficacy, and physician-patient choice.

h. Strict post-marketing surveillance must be followed

- The traceability of SEBs must be assured through unique names.
- A registry, similar to or integrated with those currently in use, will be required to provide longer term monitoring of each specific SEB.

Recommendation: That monitoring of SEBs must conform to the same rigorous standards as those used for brand name biologics.

Biologic Therapies Reimbursement Rating	Province	Detailed Remarks
Good	BC ON	<ul style="list-style-type: none"> • Provides Special Authority reimbursement for 8 out of 8 biologic therapies approved by Health Canada for use in rheumatoid arthritis. • Least restrictive Special Authority reimbursement criteria (e.g. fewest other medication failures required, and no interference in prescribing order). • Shortest wait times for initial processing of Special Authority reimbursement applications. • Fewest number of Special Authority reimbursement renewal applications required. • Formal or informal appeal mechanism in place for Special Authority reimbursement coverage denials.
Average	AB SK QC NB NS NFLD NIHB NU NT	<ul style="list-style-type: none"> • Provides Special Authority reimbursement for 7 out of 8 biologic therapies approved by Health Canada for use in rheumatoid arthritis. • Somewhat restrictive Special Authority reimbursement criteria (e.g. other medication failures required, some interference in prescribing order). • Longer wait times for initial processing of Special Authority reimbursement applications. • Special Authority reimbursement renewal applications required before one full year of coverage expires. • No transparent appeal mechanism in place for Special Authority reimbursement coverage denials.
Poor	MB PEI YT	<ul style="list-style-type: none"> • Provides Special Authority reimbursement for 6 or fewer out of 8 biologic therapies approved by Health Canada for use in rheumatoid arthritis. • Overly restrictive Special Authority reimbursement criteria (e.g. other medication failures required, interference in prescribing order). • Longest wait times for initial processing of Special Authority reimbursement applications. • Special Authority reimbursement renewal applications required before one full year of coverage expires. • No appeal mechanism in place for Special Authority reimbursement coverage denials.

Six jurisdictions have moved in the rankings since May 2010:

ON has gone up from Average to Good:

- In 2010, the province covered five out of seven biologics for RA
- In 2012, it now covers eight out of eight
- While substantial progress has been made recently, some delays remain in accessing biologics in a timely manner
- The province has also imposed onerous and overly restrictive criteria for public reimbursement on one of the funded agents

SK has gone down from Good to Average:

- In 2010, the province covered five out of seven biologics for RA
- In 2012, it now covers seven out of eight

NFLD, NU, NT and NIHB have gone up from Poor to Average:

- In 2010, these four public programs covered four out of seven biologics for RA
- In 2012, they now cover seven out of eight

NOTE: Transparency remains an issue amongst all of the public drug plans. For example, none of them publish information regarding how quickly the RA biologics can be accessed. This should be available to all patients and clinicians, with regular and timely updates.

9. Summary

As noted in 2010, biologics as a group are highly effective in the treatment of RA being efficacious in early RA, methotrexate inadequate responders and tumor-necrosis factor biologics inadequate responder patients⁷¹. There are also well-described evidence-based guidelines for the treatment of RA^{13,71,72}.

In the last two years, there has been improvement by some jurisdictions in Canada in terms of better access to RA biologics. This represents positive progress. But significant challenges remain. Unequal patient access across the country remains an unfortunate hallmark of these treatments, as do delays and barriers within the public plans themselves. No province or territory has sought to emulate British Columbia, which allows for the input of experts when applications for funding are being reviewed, invites formal patient and caregiver input onto the review process of biologics and ensures a measure of consistency and transparency in reimbursement decisions.

The emergence of subsequent entry biologics poses an additional challenge to leveling the field in RA treatments. With each of the public drug plans ultimately deciding the issue of interchangeability, it will be important to ensure, with renewed commitment, that biologics for RA are equitably and appropriately funded.

Again, we welcome the increased options that access to all biologics will afford RA patients and their physicians across Canada.

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