ARTHRITIS ALLIANCE OF CANADA
"HOT TOPIC" REVIEW

October 2016

Biosimilars
Update to original SEB Hot Topic April 2015

Biosimilars Update

Since the last AAC Hot Topic on subsequent entry biologics (SEBs), provincial formularies and private health insurers have begun providing reimbursement listing for the first biosimilars approved in Canada. Both public and private payers are considering biosimilars as a key element in their mandates to list cost-effective drug treatment that are both clinically meaningful to patients and conducive to long-term cost reductions and drug plan sustainability.

Through the pan-Canadian Pharmaceutical Alliance (pCPA), provincial and territorial public drug plans negotiated a significantly lower transparent list price for Inflectra (infliximab); according to the pCPA this will enable savings for public formularies that can be reinvested into other priorities. In April 2016, the pCPA released its First Principles for Subsequent Entry Biologics to guide negotiations and inform expectations of biosimilar manufacturers, as the pCPA works towards establishment of a biosimilars policy framework.

Health Canada has informed stakeholders that it intends to announce its adoption of the term "biosimilar" this fall when it releases a new guidance document. In recognition of this name change, the AAC is now using the term "biosimilars" and is reflected in this update.

Biosimilars offer patients and physicians another choice in the treatment of inflammatory arthritis. The AAC community is increasingly being called upon to provide information and insight for the emergence of biosimilars on behalf of Canada's 600,000 patients living with inflammatory arthritis. To help you, we provide you this update to the AAC Hot Topic paper and the latest information on biosimilars in Canada.

What are biosimilars?

Health Canada defines biosimilars as a "biologic drug that enters the market subsequent to a version previously authorized in Canada, and with demonstrated similarity to a reference biologic drug."

While relatively new to Canada, biosimilars have been approved for use in inflammatory arthritis in Europe since 2013.

The first biosimilars in Canada

Inflectra (infliximab) is a biosimilar version of infliximab based upon the reference product Remicade (infliximab). It was issued a Notice of Compliance (or "approved") by Health Canada in 2014 for the treatment of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and plaque psoriasis and recommended for listing by the national Common Drug Review.

Brenzys (etanercept) is a biosimilar version of etanercept based upon the reference product Enbrel (etanercept). It was issued a Notice of Compliance by Health Canada on August 31, 2016 for the treatment of patients with rheumatoid arthritis and ankylosing spondylitis.

Health Canada has stated that originator biologics and biosimilars are not declared to be pharmaceutically or

therapeutically equivalent. Health Canada does not support automatic substitution and does not recommend interchangeability of the biosimilar and the originator biologic.

Are patients with existing approvals for Remicade (infliximab) required to transition to Inflectra (infliximab)?

Health Canada recommends that physicians, in consultation with their patients, make well-informed choices when considering transitioning a patient's biologic medicine. Currently, payers are not mandating transitioning between infliximab and another molecule.

In terms of transitioning, the following bodies within the North American arthritis community have issued guidelines on this subject:

- Canadian Rheumatology Association (CRA) – The CRA position is there should not be interchangeability between a biosimilar and an innovator molecule. Further, there should not be substitutions from one biologic to another including biosimilar and innovator molecule.

- American College of Rheumatology (ACR) – One of the ACR's key principles in its guidelines document (which was published before biosimilars had been approved in the U.S.) is that "if a RA patient has low RA disease activity or is in clinical remission, transitioning from one therapy to another should be considered only at the discretion of the treating physician in consultation with the patient. Arbitrary transitioning between RA therapies based only on a payer/insurance company policy is not recommended."

What is the funding status of Inflectra with private health insurers?

All private health insurers have listed Inflectra (infliximab).

Greenshield and a number of other small insurers have criteria that mandates patients newly prescribed infliximab to get infliximab (Inflectra) in place of infliximab (Remicade) for rheumatoid arthritis, psoriatic arthritis, and ankylosing arthritis.

As of August 1, 2016, Remicade (infliximab) remains in first tier for all indications with a number of major insurers.

What is the current status of biosimilar naming?

Arthritis consumer and healthcare professional groups have called for distinct non-proprietary and brand naming for any and all biosimilars entering the Canadian marketplace. They did so because of the need to minimize confusion about which medication was being prescribed or taken, and, equally important, to accurately attribute adverse events to the appropriate product (biosimilar or originator biologic).

In late 2015, the WHO[1] and the United States American Food and Drug Association (FDA)[2] both released similar proposed guidance on naming - to add a unique identification code, consisting of four random consonants, to the existing non-proprietary name (e.g. infliximab wxyz). The WHO guidance also recommends that regulatory agencies like Health Canada, can add in two numerical digits as a "check-sum". Health Canada is currently reviewing the WHO proposed guidance.

[1] http://www.who.int/medicines/services/inn/WHO_INN_BQ_proposal_2015.pdf
[2] http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm459987.pdf

What is the current funding status of Inflectra with public formularies?

Inflectra (infliximab) is under review and has been approved for patients newly prescribed infliximab ("new starts") in jurisdictions across Canada.

Quebec
Effective February, 2015, RAMQ covers Inflectra (infliximab) and REMICADE for the treatment of eligible rheumatology and dermatology indications – rheumatoid arthritis, psoriatic arthritis, ankylosing arthritis, plaque psoriasis – at a Maximum Allowable Cost, whereby physicians and patients may choose Inflectra or REMICADE and the province obtains equal cost savings.

British Columbia
Effective February 19, 2016, PharmaCare covers Inflectra (infliximab) for the treatment of eligible rheumatology and dermatology indications – rheumatoid arthritis, psoriatic arthritis, ankylosing arthritis, plaque psoriasis - according to existing Limited Coverage criteria. All Special Authority (SA) requests for coverage of infliximab for infliximab-naïve patients requiring the drug for rheumatoid arthritis, psoriatic arthritis, ankylosing arthritis and plaque psoriasis will be approved for the Inflectra (infliximab) brand of infliximab only. Patients whose initial Special Authority was received before February 19, 2016, will be eligible for coverage of Remicade (infliximab).

Coverage of these drugs is subject to the rules of a patient's PharmaCare plan, including any annual deductible requirement. Retroactive coverage cannot be provided for prescriptions filled before Special Authority approval is in place.

Ontario
Effective February 25 2016, Inflectra (infliximab) was added to the Ontario Drug Benefit (ODB) Formulary as a Limited Use (LU) benefit for the treatment of severe rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis.

Patients who have an existing Exceptional Access Program (EAP) approval for Remicade (infliximab) can continue to receive Remicade (infliximab) for the duration of the EAP approval period. The ministry will also consider EAP renewal requests for Remicade (infliximab) for patients with existing EAP approvals.

The Limited Use (LU) criteria for Inflectra (infliximab) will apply to both new and existing patients with severe rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and plaque psoriasis.

Claims for Inflectra (infliximab) will be reimbursed under the ODB program when prescribed in accordance with the LU criteria and accompanied by a valid, fully completed prescription with the appropriate LU documentation (RFU code).

In March 2016, the Ontario Rheumatologist Association published this communication on their website, clarifying some special populations where patients newly prescribed Remicade (infliximab) will be eligible for funding under EAP in Ontario:

- Sub-populations:
  New starts for juvenile idiopathic arthritis (JIA) – all subtypes and both adult and pediatric Uveitis (non-infectious ocular inflammatory disease) who meet EAP criteria will continue to receive Remicade (infliximab).
- A patient who is on Remicade (infliximab) prior to February 25, 2016 and who meet EAP criteria will continue with Remicade (infliximab). At this time there is no mandatory transitioning.
- Clients age <65 previously on Remicade (infliximab) paid for by private insurance who turn 65 and meet

EAP criteria are eligible to continue with Remicade (infliximab), without a mandatory transition to Inflectra.

Alberta
Effective April 1, 2016, all new Special Authorization requests for the treatment of ankylosing spondylitis, plaque psoriasis, psoriatic arthritis or rheumatoid arthritis for infliximab naive patients are assessed for coverage with Inflectra.

Remicade (infliximab) will not be approved for patients, with ankylosing spondylitis, plaque psoriasis, psoriatic arthritis or rheumatoid arthritis, newly prescribed infliximab; however, coverage for Remicade (infliximab) will continue for patients who are currently well maintained on Remicade (infliximab) and are considered a 'responder' as defined in criteria.

Manitoba
Effective April 18 2016, Inflectra (infliximab) was added to the Manitoba Drug Benefits and Interchangeability Formulary for the treatment of rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis.

All Special Authority (SA) requests for coverage of infliximab for infliximab-naïve patients requiring the drug for rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis will be approved for the Inflectra (infliximab) brand of infliximab only. Patients whose initial Special Authority was received before April 18, 2016, will be eligible for continued coverage of Remicade (infliximab).

Saskatchewan
Effective May 1, 2016, under the Non-Interchangeable Exception Drug Status Program (EDS), infliximab (Inflectra) is authorized for the treatment of ankylosing spondylitis, plaque psoriasis, psoriatic arthritis or rheumatoid arthritis. The listing allows patients, with ankylosing spondylitis, plaque psoriasis, psoriatic arthritis or rheumatoid arthritis, newly prescribed infliximab ("new starts") to start with Infliximab (Inflectra) or infliximab (Remicade).

Nova Scotia
Effective June 1, 2016, under the Exception Status Drug program, infliximab (Inflectra) is authorized for the treatment of Ankylosing Spondylitis, Plaque Psoriasis, or Rheumatoid Arthritis.

For infliximab-naïve patients whose infliximab therapy is initiated after June 1, 2016, infliximab (Inflectra) will be the product approved for rheumatoid arthritis and ankylosing spondylitis.

New Brunswick
Effective June 1, 2016, under the New Brunswick Drug Plans Special Authorization Program, infliximab (Inflectra) will be approved for ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, and rheumatoid arthritis.

Please note that all Special Authorization (SA) requests for reimbursement of infliximab for infliximab-naïve patients for ankylosing spondylitis (AS), psoriatic arthritis (PsA), and rheumatoid arthritis (RA).

RA, AS and PsA will be approved for the Inflectra® brand of infliximab only. Patients who received SA approval for the Remicade® brand of infliximab before June 1, 2016 will continue to have this brand covered. They will also be eligible for reimbursement of infliximab (Inflectra).

Prince Edward Island
Effective June 27, 2016, under the High Cost Drug Program and Catastrophic Drug Program, infliximab (Inflectra) will be the product approved for ankylosing spondylitis, plaque psoriasis, psoriatic arthritis, and rheumatoid arthritis.

For infliximab-naïve patients effective June 27, 2016 or later, infliximab (Inflectra) will be the product approved for the ankylosing spondylitis, plaque psoriasis, psoriatic arthritis or rheumatoid arthritis. Naïve patients are defined as those not on maintenance infliximab therapy (including those receiving induction therapy) as of the effective date of coverage on PEI (June 27, 2016).

How can you stay informed and involved?

Biosimilars will have an increasing role to play in the Canadian health system. How can you stay informed and involved?

- We encourage you to provide your comments and questions to the AAC office
- Feedback received will be compiled for consideration in future updates
- Continue to share perspectives and experiences around this important health topic
- Help educate your community – they will be affected by the arrival of biosimilars
- Understand how biosimilars are assessed and listed on public and private formularies

About The Arthritis Alliance of Canada

The Arthritis Alliance of Canada, formerly the Alliance for the Canadian Arthritis Program (ACAP), was formed in 2002. Its goal is to improve the lives of Canadians with arthritis.

With more than 30 member organizations, the Arthritis Alliance brings together arthritis health care professionals, researchers, funding agencies, governments, voluntary sector agencies, industry and, most importantly, representatives from arthritis consumer organizations from across Canada. While each member organization continues its own work, the Alliance provides a central focus for national arthritis-related initiatives.

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