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Canadian Rheumatology Association position statement on Biologic Access

Biologic medications have become a cornerstone of the treatment for rheumatic diseases in adults and children in Canada. As more biologic options become available, including biosimilars, the ability of patients to access different biologic agents or switch between different formulations is important. The choice of biologic agent is a complicated decision made in a collaborative discussion between a physician and a patient and considers many variables including diagnosis, disease severity, comorbid conditions, and patient specific factors such as preferred administration mechanism and access to medical care (e.g. rural, urban or remote location). Many biologics are administered via subcutaneous injections and studies have shown that injection pain can lower both medication adherence and patient quality of life. Different factors are thought to contribute to injection pain (e.g. needle size, pH, volume/concentration, preservatives, or mechanism of injection) [1]. The composition of biologic injections including additives such as citrate are also thought to impact injection pain, and this has led to the development of low citrate or citrate free formulations.

The CRA encourages rheumatologists to provide the best care for individual patients and be mindful of cost savings for the benefit of society as a whole. When there is a choice available between biologics (including between an originator and biosimilar of the same molecule) then the rheumatologist should consider choosing the most cost-effective option in the context of patient specific factors (e.g. pregnancy planning, comorbidities etc). Regarding transitioning between formulations of the same agent, it is imperative that any substitution or transition/change should result in no additional cost to the patient. The CRA recognizes the administrative challenges that patients may experience in accessing a biologic agent and therefore strongly encourages industry to provide and/or maintain patient support programs.

1. Biologic naïve patients: For patients new to a specific biologic, cost effectiveness and patient specific factors such as comorbidities and access to care should be considered when there is an available choice between the originator biologic and one or more biosimilars.

2. Transitioning and/or switching biologics for patients on existing biologic treatment: A respectful and informed conversation between the rheumatologist and patient must occur prior to transitioning/switching from an originator biologic to a biosimilar or vice versa. Any switch or new start with a biologic must consider those agents which are best tolerated and have the appropriate formulation.

3. Biosimilar Substitution by someone other than the prescriber:
a. Advanced notification of an intended substitution must be provided to the prescribing rheumatologist and patient.
b. There will be no substitution without an informed consultation between the patient and the prescribing rheumatologist prior to any treatment change. Thus, when a substitution is proposed, at least 6 months is required to allow sufficient time for a prescriber - patient dialogue to occur.
c. In the event of substitution, the patient's current biologic must continue to be provided until access to the alternate formulation is confirmed and available.

4. Tolerability of biologics
a. The CRA encourages payers to have a process in place to allow the patient to revert to the original biologic agent in a timely fashion in the event of a clinically relevant flare of the disease after an appropriate trial with up to two biosimilars; or in the event of intolerance to the new formulation and alternate appropriate biosimilars are not available (e.g., citrate free, higher concentration or pediatric appropriate formulations).
b. The CRA strongly recommends that, when applicable, private and public payers ensure access to formulations that are appropriate for pediatric dosing and treatments that are formulated to reduce injection site pain (e.g. at least one citrate-free biologic). In addition, if a patient is experiencing injection pain, we strongly recommend that the physician have the choice, in conversation with the patient or caregiver, to switch to options that will reduce pain.

Terminology regarding Biologics and Biosimilars [2,3]

1. **Biologic disease-modifying antirheumatic drugs (in this document referred to as "biologics")**: large complex molecules produced through biotechnology and used to treat rheumatic diseases [3]

2. **Biosimilar**: a biological product that is highly similar and has no clinically meaningful differences from an existing FDA-approved reference product

3. **Substitution**: is the FDA-preferred term that refers to a change in treatment by someone other than the prescriber and may be regulated by the law. Substitution is also termed nonmedical or administrative substitution. [2]

4. **Transitioning and changing:** an intentional therapeutic alteration to a biosimilar initiated by the health care provider in partnership with the patient. [2]

5. **Switching**: this term is used, according to the US Biologics Price Competition and Innovation (BPCI) Act of 2009, when transitioning to or from a biosimilar which has been designated interchangeable [2]

6. **Interchangeability**: refers to a status that may be granted to a biosimilar that is "expected to produce the same clinical result as the reference product in any given patient". To date there is no product that has been designated interchangeable in Canada. This status can be achieved by results of post-marketing surveillance and at least one prospective controlled switching study requiring subjects to be switched over at least three times in the switching arm. [2]

References:
[1] Junker S, Ebert O, Bartsch R. A Systematic Literature Review of Injection Site Pain Perception in Adult Patients Treated with Citrate-Free and Citrate-Containing Biologic Agents. Curr Rheumatol Rev. 2023 Jun 5;19(3):303-313. doi: 10.2174/1573397118666220829123713. PMID: 36043729; PMCID: PMC10433360.

[2] Bridges SL Jr, White DW, Worthing AB, Gravallese EM, O'Dell JR, Nola K, Kay J, Cohen SB; American College of Rheumatology. The Science Behind Biosimilars: Entering a New Era of Biologic Therapy. Arthritis Rheumatol. 2018 Mar;70(3):334-344. doi: 10.1002/art.40388. Epub 2018 Feb 7. PMID: 29411547.

[3] https://www.fda.gov/files/drugs/published/Biological-Product-Definitions.pdf