

## Making Sense of New Treatment Options for Autoimmune Diseases

# SEB

Subsequent Entry Biologics

### Introduction

The use of biologic response modifiers or “biologics” (medicines created by biological processes, as opposed to chemically), has had a profound impact on patient care. Biologics have been developed, Health Canada-approved and marketed for a range of serious and life threatening diseases, such as autoimmune forms of arthritis (rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis), cancer, multiple sclerosis and rare metabolic disorders, to name a few. They include such diverse protein products as monoclonal antibodies, cytokines, protein hormones, gene therapies, vaccines, and blood and blood components.

Biologic therapies are complex molecules derived from unique living organisms and cell lines making them complicated to produce. The molecules themselves are composed of a large number of molecular components and are of a large molecular weight, which is why they are administered by injection or intravenously (directly into a vein). Small differences in the production of biologics can yield vastly different products with unique effectiveness and safety implications.

Ensuring that Canadians who most need treatment with biologic medications have provincial reimbursement access is an ongoing challenge. But more recently, another issue has emerged that directly impacts the principle of patient choice in this area – Subsequent Entry Biologics.

As patents expire over the next decade for “brand name” biological medicines (like Enbrel®, Remicade® and Humira®), Subsequent Entry Biologics (or “SEBs”) are being developed. Health Canada and provincial drug formulary managers have begun to consider how to regulate these products, and Canadians need to understand the complexities behind the development, regulation and provincial drug formulary listings of SEBs.

In this special BC edition of JointHealth<sup>TM</sup> monthly, we address the need for more education about SEBs to help you make informed judgments on the value of biologics and the scientific, ethical and economic issues that they raise.

### Questions + Answers about SEBs

#### What is a Subsequent Entry Biologic or “SEB”?

A Subsequent Entry Biologic is used to describe a biologic product that is similar to a brand name biologic that has gone off patent. Other terms used to describe SEBs include “biosimilar”, “similar biological medicinal product”, or “follow-on protein products”. They are not “equivalent” to well-researched “brand name” biologics.

#### How does Health Canada review a SEB for safety and efficacy?

A manufacturer wishing to obtain a license to sell a SEB in Canada must apply to Health Canada for a review of the product’s safety and efficacy. Unlike for manufacturers applying for a review of a unique, “brand name” biologic, SEB manufacturers are allowed to submit information regarding safety and efficacy that is borrowed from a previously approved biologic because it is deemed “similar”.

Regulatory agencies (like Health Canada) around the world are today struggling to find a balance with respect to how much SEB manufacturers can rely on research information from the brand name biologic medication manufacturer in applying for their own approval.

#### Why should Health Canada’s review process for SEBs be of concern to Canadian patients?

A SEB is only “similar” to the original brand name yet the review process is far less demanding.

The SEB manufacturer does not have access to the brand name biologic’s manufacturing process history, which means that Health Canada is only seeing a relatively small amount of safety and efficacy information compared to the brand name biologic to which it is similar.

#### How many SEBs have been approved by Health Canada?

So far, only one has received a Health Canada “notice of compliance” or a “license” to be marketed in Canada.

In Europe, where one regulatory agency (European Medicines Agency or “EMA”) reviews drugs for safety and efficacy, five SEBs have either been withdrawn or were rejected. No EU Member State allows automatic substitution of SEBs for the brand name comparator. This highlights the need for Health Canada to require sufficient safety and efficacy data for the approval of SEBs in order to protect patient safety, which should be of paramount importance.

#### What are Health Canada’s and provincial drug plans’ policies regarding SEBs?

Health Canada has declared that SEBs are not substitutable for brand name biologics, however, provincial drug plans are still in the process of deciding how to handle government reimbursement of SEBs and policies have yet to be developed.

No EU Member State allows automatic substitution of SEBs for the brand name comparator.

# ACE recommendations on SEB regulation and public drug formulary reimbursement in Canada

ACE believes patient safety and choice must be the primary concern of SEB regulation in Canada. Although Health Canada has stated that SEBs are not equivalent to brand name biologics, that does not prevent the publicly funded drug plans from treating SEBs the same as generic chemical molecules for reimbursement purposes. With no policy framework in place at the provincial level and SEBs on the market, and since SEBs are “similar” and not the same as the innovator product, ACE makes the following recommendations:

## **1 : SEBs must have an acceptable safety profile:**

Substantial clinical trial data should be required to demonstrate a satisfactory safety profile for each SEB product. A SEB manufacturer should be required to provide Health Canada the same depth of information on their product’s safety and efficacy as the brand name product to which it claims similarity.

Health Canada should require that there already exists a Canadian-approved brand name biologic to which the SEB in question can be compared for similarity.

## **2 : SEBs are not interchangeable 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 their brand name biologic, provincial drug plans have yet to formulate the same policy.

Doctors 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. Decisions to substitute one similar product with another should only be made at a physician’s discretion.

## **3 : Each biologic product must have a unique product name:**

Each SEB product must have unique and distinguishable names and a distinct name under the International Nonproprietary Names (INN) Program of the World Health Organization. Given the fact that SEB products are not identical to innovator products and could have significantly different clinical outcomes for patients, physicians, pharmacists, and nurses 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 governments efforts to closely monitor adverse events. Without distinct names, patients, physicians and pharmacists could become confused, leading to inadvertent product substitution. Consequently, if there are fluctuations in patients’ responses, it could become more difficult to determine the source and therefore complicate the tracking of adverse events.

## **4 : Cost must not override safety:**

The cost of producing SEBs is approximately 15-30% 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.

Preferential listing of SEBs on provincial formularies should be discouraged if it is at the expense of patient safety, proven product efficacy, and physician-patient choice.

## **5 : Strict post-market surveillance must be followed:**

Monitoring of SEBs must conform to the same rigorous standards as those used for brand name biologics. The traceability of SEBs must be assured through unique names. Repeated, uncontrolled switching between SEBs and the brand name biologic to which they are similar must be avoided in order to ensure adequate safety surveillance.

**ACE supports the introduction of SEBs to treat people with autoimmune arthritis who rely on publicly-funded drugs, but only if they are assured the choice between a SEB and the brand name biologic or other biologic that may better fit a patient’s needs. It is vitally important that brand name biologics and SEBs receive equal consideration on publicly funded drug formularies in order to best meet the needs of those requiring these highly effective therapies.**

## What can ACE members and JointHealth™ subscribers do to raise awareness about SEBs in Canada?

- Share the information in this special edition of JointHealth™ monthly with your rheumatologist or the health professional who helps you manage your arthritis
- Share the information in this special edition of JointHealth™ monthly with others in your arthritis community
- Encourage others you know with arthritis, and their family members and friends, to share this important information with their local elected official
- Write to the Minister of Health Services and ask them for their assurance that BC PharmaCare will list SEBs in a non-preferential manner (equal to brand name biologics) on the province’s drug formulary

To learn more about SEBs, please visit the following links:

Arthritis Consumer Experts and JointHealth™:  
[www.jointhehealth.org](http://www.jointhehealth.org)

International Alliance of Patient Organizations or “IAPO”:  
[www.patientsorganizations.org/biosimilars](http://www.patientsorganizations.org/biosimilars)

Health Canada:  
[www.hc-sc.gc.ca/dhp-mpps/brgtherap/applic-demande/guides/seb-pbu/notice-avis\\_seb-pbu\\_2010-eng.php](http://www.hc-sc.gc.ca/dhp-mpps/brgtherap/applic-demande/guides/seb-pbu/notice-avis_seb-pbu_2010-eng.php)

### Who we are

Arthritis Consumer Experts (ACE) provides research-based education, advocacy training, advocacy leadership and information to Canadians with arthritis. We help empower people living with all forms of arthritis to take control of their disease and to take action in healthcare and research decision making. ACE activities are guided by its members and led by people with arthritis, leading medical professionals and the ACE Advisory Board. To learn more about JointHealth™ and Arthritis Consumer Experts (ACE) please visit [www.jointhehealth.org/about.cfm](http://www.jointhehealth.org/about.cfm)

ACE does not promote any “brand”, product or program on any of its materials or its website, or during any of its educational programs or activities.

### Disclaimer

The material contained in this newsletter is provided for general information only. It should not be relied on to suggest a course of treatment for a particular individual or as a substitute for consultation with qualified health professionals who are familiar with your individual medical needs. Should you have any healthcare related questions or concerns, you should contact your physician. You should never disregard medical advice or delay in seeking it because of something you have read in this or any newsletter.



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