Speaking with One Voice

Important Considerations for SEB Policy Development

In January 2014, Health Canada approved two subsequent entry biologics (SEBs) or biosimilars - Remsima™ and Inflectra™, both of which are biosimilar versions of Remicade™ (infliximab). They were approved for rheumatologic use for rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis and were extrapolated to psoriasis. As of June 2014, these products have not been marketed; however, they are under consideration for formulary listing.

There is a unified voice from those invested in best patient outcomes to ensure payers are aware of all the factors involved as policy and access decisions are made around SEBs. This discussion paper outlines the key areas identified by the participants of a cross-disciplinary advisory board to be addressed when considering SEBs as part of provincial/ territorial formularies. These considerations are founded on the principle that patient outcomes should be the paramount criterion for physicians, pharmacists, patients and policymakers.

Policy Requirements for Successful Introduction of SEBs

A cross-disciplinary group that included specialist physicians from dermatology, gastroenterology, nephrology, oncology and rheumatology, as well as pharmacists, patients and patient groups, identified issues of concern surrounding the introduction of SEBs. Together they speak with one voice, urging the following be considered and resolved:

- ✓ **Awareness & education of professionals and patients**
- ✓ **Robust clinical data for safety, efficacy and extrapolation**
- ✓ **Unique SEB names to avoid interchangeability and substitution without patient-physician dialogue**
- ✓ **Post market surveillance equal to innovator biologics**
- ✓ **Leadership and accountability to ensure good patient outcomes**

Background

The 2010 Health Canada *Guidance for Sponsors: Information and Submission Requirements for Subsequent Entry Biologics (SEBs)* clearly stated authorization of an SEB was not a declaration of interchangeability nor substitutability. The guidance further stated an approved SEB would become a stand-alone biologic and treated as a new drug, and extrapolation to other indications would only be considered with strong analytical data and scientific justification. At the time, it also outlined an SEB would require an individual risk management plan and a different brand name to differentiate it from other biosimilar products. There were, however, some departures from this guidance document when Health Canada approved the biosimilar versions of Remicade.

As these and future files proceed through the public policy process, those involved in patient care, access to new medicines and patient education believe strongly in speaking with one voice to ensure patients benefit from the introduction of SEBs. In June 2014 BIOTECanada hosted a cross-disciplinary meeting of specialist physicians (dermatologists,

gastroenterologists, nephrologists, oncologists and rheumatologists), pharmacists, patients and patient group representatives who together identified several areas of concern, recommending further dialogue and consideration.

Awareness and education must be components of any decision

Biologics and SEBs are complex medicines. Without a concerted effort to educate physicians who will prescribe SEBs, pharmacists who will dispense them and patients who will take them, the introduction of SEBs brings with it inherent risks. Patients, general practitioners and community pharmacists are familiar with generic products being available once a brand name patent expires. In those cases, substitution is based on proven interchangeability. There is concern however, without significant education and raising of awareness, SEBs will be viewed as "generic biologics". SEBs are not generic biologics. Biologics and SEBs are not interchangeable.

"The introduction of SEBs is a new concept for most stakeholders. People are talking about how much they don't know about this area as we go out and educate them on biosimilars."

Participants cited a low level of awareness of SEB nuances among physicians who prescribe biologics and biosimilars. Similarly, low awareness exists among community pharmacists and, to a lesser extent, hospital pharmacists and specialty clinics. Professional awareness sessions reach some but not all practitioners. Most importantly, only patients affiliated with patient support groups have had some exposure to this new area of medicine.

The challenge, then, is to ensure health care practitioners and patients understand the implications of changing between biologics and SEBs; the lack of such understanding threatens the ability of patients and physicians to make informed choices regarding care and treatment. While this lack of understanding is not necessarily at the forefront now, once the current SEBs are marketed and more are approved, the gap in knowledge will become more evident. There was discussion that patients might be unaware or confused and/or adherence rates might drop; physicians might even turn away from prescribing their biologic of choice. There was also concern that patient outcomes could be at risk.

"There needs to be greater interaction and collaboration amongst professions when you are dealing with a subject as complex as biologics and biosimilars. Communication to the patients must be consistent and as professionals it should be clear that we speak with one voice."

Robust clinical data must drive safety and efficacy discussions and any extrapolation to other indications

The choice of any therapy, including originator biologics and SEBs, should be a shared decision made between a physician and a patient, based on informed knowledge of the patient's clinical condition and safety and efficacy of the product. There is a need for more extensive data on immunogenicity and long-term safety data on new SEBs, when used alone or in combination with other medications, to give physicians the confidence to appropriately prescribe them and patients the confidence to use them.

Extrapolation to other indications without in-depth data carries implications for decisions concerning effective patient care. Given the complexities of immunogenicity, efficacy and side effects of all biologics, any extrapolation must be supported with good clinical data. Identifying potential side effects and interactions are important as is determining efficacy.

"There is a lack of clarity as to how the results of a specific study design will be used: Will efficacy of an oncology SEB tested in a curative setting be used to inform its use in a metastatic setting? The criteria for success are different for each of them and will impact real world decision-making."

Physicians prescribing SEBs will need to monitor patients closely. They bear the legal burden for their prescribing choices and rely on good data to make good decisions. These monitoring costs and the costs of treating any adverse events must be considered when evaluating the potential cost-savings of making SEBs available.

The absence of unique international non-proprietary names for SEBs threatens patient safety and post-market surveillance efforts

As discussed, there is a low level awareness of the complexities of SEBs among physicians, pharmacists and patients. Adding to this complexity is the lack of requiring a unique international non-proprietary name (INN) for the biologic and each SEB that is approved. While this matter is still under consideration at the World Health Organization, Health Canada has set protocol by allowing several biologics to share an INN.

It is very important that SEBs have unique names in order to meet the pharmacovigilance required by the subtle differences in dosage, efficacy and immunogenicity of these products. With low awareness of the complexity of biologics and SEBs, and the ingrained perception of brand name medicines eventually being available as generics, the presumption of interchangeability of SEB with its originator biologic, and automatic substitution are very real concerns.

"The concern is that if a non-proprietary name is the same, pharmacists will assume it is a generic due to lack of knowledge of biologic drug complexity."

The lack of a unique name also compromises post-market surveillance of adverse events. Without a distinct name, and with the potential of interchangeability, attributing an adverse event to a specific manufacturer or incorrectly labeling it a class effect become real and potentially dangerous possibilities. Physicians and pharmacists will be unable to easily distinguish these; patient health will be impacted, sometimes significantly. The use of SEBs requires pharmacovigilance/risk management programs equivalent to innovative biological medicines.

"Having gone through a pretty severe storm a decade ago with PRCA, we have had the opportunity to see how a simple change in manufacturing of a rubber stopper caused a significant adverse event in the care of patients. This has created a lot of apprehension about the entry of SEBs based on our basic principle of doing no harm."

Leadership in balancing patient risk with health care system cost savings

SEBs are a welcome addition to treatment options and, as anything new, must be fully understood. The anticipated cost savings with SEBs available are important, but must be carefully balanced by health outcomes and the overall cost to the health care system. Increased access to biologics by patients because of reduced costs must also be weighed against the potential of physicians stepping away from prescribing biologics and SEBs because of inherent risk (lack of robust clinical data across indications, fear of substitution) of losing control and impacting patient outcomes.

"The drop in price is why everyone is interested [in listing SEBs]. But how do we make that happen in a safe manner so that there is flexibility and independence and choice for patients and clinicians is needed? If it is regulated, then we as a clinical community must say that we don't agree with this. We must be a unified voice on this issue."

Finally, there is a need for leadership and a clear assignment of accountability for patient outcomes as SEBs enter the Canadian health care system. Health care practitioners are ultimately liable for the decision to prescribe, pharmacists to dispense and patients to adhere to their treatment regime. The role of health policy makers is to deliver an SEB reimbursement policy environment based on good science, management of patient risk and responsibility for health care costs. All three of these pillars must be taken into account.

Meeting Participants

The cross-disciplinary dialogue included those listed below and revealed a high degree of consensus about the areas that must be addressed prior to new SEB products entering the Canadian market. The group strongly endorsed an inter-professional approach to dealing with many of the issues.

Discipline	Name	Organization
Gastroenterology	Dr. Jamie Gregor	Victoria Hospital
Nephrology	Dr. Daniel Sapir	Daniel Sapir Medical Professional Corporation
Nephrology	Dr. Sanjay Pandeya	Halton Healthcare Services
Rheumatology	Dr. Arthur Karasik	Ontario Rheumatology Association
Rheumatology	Dr. William Bensen	St. Joseph's Hospital/McMaster University
Rheumatology	Dr. Vandana Ahluwalia	William Osler Health System, Ontario Rheumatology Association
Dermatology	Dr. Neil Shear	Sunnybrook Health Sciences Centre
Pharmacist	Carolyn Whiskin	The Charlton Centre For Specialized Treatment
Pharmacist	Allan Malek	Ontario Pharmacists Association
Patient	Dawn Richards	Canadian Arthritis Patient Alliance
Patient Association	Andrew Jones	The Arthritis Society
Patient Association	Aida Fernandes	Crohn's and Colitis Canada
Patient Association	Colleen Savage	Cancer Advocacy Coalition of Canada
Patient Association	Robert Corbeil	Canadian Psoriasis Network

For more information on biologics and subsequent entry biologics please visit BIOTECanada at www.biotech.ca