Manitoba Subsequent Entry Biologics Forum Report

LSAM
Life Science Association of Manitoba

THE SCIENCE OF LIVING BETTER.

EXECUTIVE SUMMARY

When lay people think of pharmacy, they generally think of pills. But the cutting edge of the pharmacy today is found in biologics. Biologics are complex medical products derived from a variety of sources related to living organisms and created through advanced biotechnological techniques. They are administered to patients through infusion or injection, requiring some clinical support for a treatment regimen. Biologics offer medical treatment for chronic conditions ranging from cancer to rheumatoid arthritis to inflammatory bowel conditions, providing an improved quality of life to patients who previously suffered significant impairments.

Subsequent Entry Biologics ("SEBs"), also known as "biosimilars" or "follow-on biologics" in Europe and the USA, are follow-on versions similar to an original biologic drug developed after the patent on the innovator drug has expired. The advent of SEBs poses significant challenges and opportunities to health care policy makers in Canada. The LSAM's Subsequent Entry Biologics Forum explored these issues with presentations from the perspective of patients, policy makers at both the provincial and federal government levels, researchers, academics, and the industry.

A panel discussion at the event touched on areas such as the monitoring of SEBs in the market, innovation and consultation with patients and policy makers. As the voice of the organizational nucleus of the life science industry in Manitoba, LSAM is providing this report which contains a summary of the presentations and discussions at the Forum, and a set of recommendations around continued consultation on this issue.

THE SEB POLICY CONTEXT

Canada's public health care system faces many challenges to evolve as we move further into the twenty first century. Ageing populations with increasing service expectations offer a challenge to the system from one side, while relentless medical innovation offers exciting opportunities from another side. Some of these opportunities can come with a high cost, while offering significant benefits to patients. The area of public health care policy that perhaps captures these broad dual pressures more than any other is pharmacy and the provincial systems of publicly-funded provision of medication for Canadians.

Canada spends 10% of its GDP on public health care . Total health spending in Canada exceeded $200 billion in 2011. In 2012, governments and public sector agencies spent $145.1 billion on health care, and the amount was forecast to be $151.5 billion in 2014 . Within this same period expenditure on drugs constituted the second-largest category of health spending, forecast overall to be $33.9 billion in 2014, $12 billion of which would be spent by public sector agencies , including Canada's various provincial pharmacare plans.

Canada's health system is also home to significant medical innovation that is improving outcomes for patients. Numerous innovations in medical care coming available to larger and larger proportions of the Canadian population. Canadians are living longer. In 2009 Canadian life expectancy was 81.1 years, an increase from 74.9 years in 1979 . Health care spending is increasing, but people are getting more out of the health care system.

Manitoba policy makers are not immune to these trends. Manitoba's Pharmacare Program is the main public policy instrument for supporting drug costs in the provincial health system. The Manitoba government was budgeted to spend nearly $310 million on its Pharmacare program in 2015-2016 . Demographic trends, new drug technologies and increasing expectations from patients and their families are driving significant pressures on spending on the Pharmacare system. Of the myriad of new drugs available, the category of medication known as "biologics" are a material driver of increasing costs in the system.

Biologics are not easy to develop. Pharmaceutical companies must make significant investments in research & development as well as complex manufacturing in order to provide biologics. With their complex development and their clinical application, biologics are therefore very expensive, imposing costs on public pharmacare plans and patients. In Manitoba's case biologics comprise over 16% of spending in the pharmacare plan, but represent less than 1% of total prescription drug use. Patients taking biologics have reported remarkable improvements regarding relevant conditions – their lives are sometimes transformed by these very advanced, very expensive medications they will likely need to take for the rest of their lives. As demand for biologics increases, medical policy makers and stakeholders are grappling with issues of cost sustainability.

The advent of SEBs has implications for all of these policy makers and stakeholders. Generic medications have had a tremendous impact on the amounts governments and public agencies in Canada spend on pharmaceuticals. Could SEBs affect the biologics landscape in the same way?

Due to the complex nature of biologics, their manufacture and provision to patients, the employment of SEBs by Canadian health care providers raises a number of issues for the pharmaceutical treatment landscape in Manitoba. The molecular structure of SEBs is not identical to the reference biologic drug – the process involved in creating the innovators, and therefore recreating them in a "similar" fashion is still very advanced. What does this mean for regulatory approval? Patients take biologics via infusion or injection, meaning clinical support is needed. How would SEBs be distributed to patients?

The Life Science Association of Manitoba (LSAM) is in an excellent position to highlight the different perspectives of stakeholders and policy makers as they consider the entry of SEBs into Manitoba and the possible impacts SEBs might have on the health care system and the patients and families who count on it. LSAM gathered a number of significant stakeholders together – representing pharmaceutical businesses, the life sciences industry, academic expertise, health care providers, policy makers and policy stakeholders at the provincial and national level – for its "Subsequent Entry Biologics Forum." This report provides a synopsis of the forum and an overview the diverse discussions at the event.

SUBSEQUENT ENTRY BIOLOGICS FORUM

LSAM hosted the Subsequent Entry Biologics Forum on January 20, 2015. The Forum was designed to spark a constructive dialogue – what are the issues, what are the challenges and what are the opportunities that SEBs present to Manitoba's pharmaceutical landscape? LSAM built on its strong connections to a wide assortment of stakeholders and build an event to kick-start a constructive dialogue on the issues around SEBs.

The first presenter was Cheryl Koehn, Founder and President of Arthritis Consumer Experts, a national organization that provides information, education and support programs to people living with arthritis. Cheryl is a passionate advocate for people living with arthritis and she brought this passion to the forefront in her presentation. Cheryl spoke from personal experience of the devastating impact that chronic arthritis can have on the lives of those who suffer from it. She described the challenge in the community of waiting for medication to come along, and when biologic treatments became available they were like "Cinderella – a transformation from a rags to a satin ball gown."

Cheryl's message was that in the context of discussion around SEBs, the voice of patients should come first. She noted the focus among policy makers and stakeholders on the significant costs involved with biologic medications. Her view was that policy makers should take a more global view of the costs to the system, that money spent on the medication should be judged not just against the budget of a given pharmacare program, but against overall costs to the economy. When someone suffering from chronic arthritis received biologics they are more productive in the economy, and require less attention from other areas of the medical system.

Cheryl argued this broader consideration should be the context in which the arrival of SEBs to Canada is contemplated. Building on this, she moved to the questions around regulatory approval of SEBs. She stated she was not opposed to them coming to the market, but they must be thought of as a new class of medications. SEBs are not the same as generics, and the possible harm coming from an SEB that is not tested properly is real. She stressed patient safety and choice, and maintained that patients should have a voice to ensure the process for approval SEBs is safe and that policy around their implementation takes a broad view of the relevant costs of chronic conditions as well as biologics into account.

The next presenter at the forum shifted the perspective over to the regulatory side of the equation. Dr. Agnes Klein is Director of the Centre for Evaluation of Radiopharmaceuticals and Biotherapeutic Products in Health Canada's Biologics and Genetic Therapies Directorate. There are more than 20 clinical trial applications for SEBs in Canada, and Dr. Klein shared an overview of Health Canada's approach to the approval of SEBs for use.

Health Canada recognizes that SEBs are developed through complex processes, and has established a process they feel is reflective of this complexity. SEBs are subject to a regulatory approval process that is more detailed than that followed for generic medications, but still not exactly the same as an "innovator" biologic is subjected to.

For Health Canada approval an SEB has to demonstrate that its molecular structure and function are highly similar to the original biologic (the "reference product") and this must be backed up with clinical trials in sensitive populations. Health Canada does allow the extrapolation of data gathered from other studies for SEBs, with the expectation that appropriate data and rationales are provided so the extrapolation is relevant and safe.

This process can end with Health Canada giving an approval for some medical purposes but not others, even if the same SEB has been approved for other purposes in other jurisdictions. To provide an example of the process Dr. Klein provided a brief overview of the SEB infliximab, which has been approved in Canada for treatment of some conditions (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and plaque psoriasis) but not yet approved for others (adult and pediatric Crohn's disease and ulcerative colitis).

Dr. Klein's presentation also touched on issues of "immunogenicity" – the immune system response that biologics can create in patients. A response from a patient's immune system to a biologic medication can create a very negative outcome for a patient, and the possibility of immunogenicity is an issue SEB stakeholders watch closely. Dr. Klein stressed that immunogenicity is difficult to predict, and outlined Health Canada's position that a risk-based evaluation strategy should be followed, that a post-marketing risk plan is required, and stresses that the newest and most sensitive methods should be employed for assays used to detect immunogenicity.

The LSAM forum then moved to discussion of the payer's perspective with a presentation from Dr. Patricia Caetano, Executive Director of the Provincial Drug Program for Manitoba Health. Dr. Caetano highlighted the challenge that biologics are making to the sustainability of the provincial drug program. She provided figures underlining the financial impact biologics have on spending in the pharmacare program – with the province of Manitoba spending $52 million (16% of the annual drug budget as of 2014-15) on these medications, which in turn represented 0.7% of total drug utilization under the plan.

Dr. Caetano highlighted the potential savings that might be possible through the use of SEBs in the Manitoba Pharmacare program, citing an example from European jurisdictions where the cost of the SEB was 30% lower than the original innovator product. She noted the current pricing approach for the innovator product sets the level for a specific approved use, and this is not changed as other uses for the drug are added. She raised the issue of "re-benching" drug prices and biologics SEBs – when might that happen, and how?

A further potential challenge was also highlighted in this presentation – the issue of infusion clinics. Biologics are often infused in a patient, and this must be done with the assistance of someone qualified to ensure it happens safely. How might SEBs be infused in Manitoba? Would an infusion clinic become necessary for the Manitoba health system, as opposed to branded infusion clinics operated by the innovator and/or biosimilar companies? And if Manitoba opened its own infusion clinic, what impact would that have, both on existing infusion by innovators, as well as the provincial health system itself?

Dr. Caetano also raised the issue of medical tourism from the United States of America. If SEBs begin to arrive in Canada in a significant way, will this mean the return of tour buses to get access to drugs which citizens of the U.S. could not afford to access themselves, with all of the related issues arising once again?

The final presentation was given by Dr. Shawn Bugden, Associate Professor from the Faculty of Pharmacy with the University of Manitoba. Dr. Bugden highlighted the key differences between generic drugs and SEBs, but also sought to explore the areas where lessons learned from generics might highlight challenges and opportunities around SEBs. To highlight his point Dr. Bugden compared small molecules in a generic medication to a bicycle, and noted that in comparison SEBs are like a jet plane. He shared an anecdote that highlighted the challenge of general understanding of the concept of "similarity" from a statistical standpoint, and how this can affect perceptions people hold of generic drugs, and how this might affect understanding of SEBs in a similar way. He noted in this context that SEBs should not be considered as interchangeable with the innovator – they are still different medications.

Dr. Bugden provided a further perspective on the financial environment that pharmacare plans are operating within, noting that in 2013 prescription drug spending growth was at its lowest point in two decades. He outlined evidenced-based principles for the assessment of SEBs, and he emphasized the importance of shared decision making and post-marketing surveillance with SEBs. His final point highlighted the continuing challenge facing policy makers – as more drugs come off patent, more SEBs are going to come along, underscoring the importance of the dialogue among stakeholders regarding the challenges and opportunities with SEBs.

PANEL DISCUSSION

With the close of Dr. Bugden's presentation, a panel discussion was established. Two more guests joined the presenters to complete the panel – Tara Bingham, Director of Government Affairs with Hospira and Lisa Chartrand, Director of Regulatory Affairs and Quality Management at Hoffman-La Roche. Questions and discussion were moderated by LSAM President Tracey Maconachie.

The Panel Discussion touched on three areas:

- *How could or should SEBs be monitored post-marketing?*
- *How often do you have to evaluate biologics and SEBs to account for manufacturer's drift?*
- *What should consultation look like?*

How could or should SEBs be monitored post-marketing?

Panel discussion on this topic noted the differences between the regulatory approaches of the USA, Europe and Canada. Panellists also shared different perspectives on the financial contexts which should be informing the overall policy discussion. It was noted that increased monitoring can actually offer increased health care benefits to patients who participate in monitoring studies.

Panellists noted that surveillance should be based on data gathered to reflect effectiveness in the "real world" as opposed to clinical studies, but also touched on the challenges involved – how can data be tracked properly with multiple products in the market? Panellists further noted the issue of surveillance isn't limited to SEBs, and the desire to have a pharmacovigilance approach that continues to evolve and provide the best data possible to all parties is an ongoing challenge. This pointed again to the importance of a dialogue among the stakeholders to ensure policy makers in Canada craft an effective approach.

How often do you have to evaluate biologics and SEBs to account for manufacturer's drift?

With regard to ongoing evaluation and manufacturing the panellists touched on differences between jurisdictions. It was noted that while Health Canada has made an approval and the Food and Drug Administration (FDA) of the USA had not yet done so, the FDA was still seen as ahead of Canada and Europe in terms of developing policy related to SEBs. Panellists noted that health policy in Canada is a product not just of the federal government, but of the different provincial governments as well, something also seen within Europe. Panellist recommended continued consultation, noting that with different jurisdictions even within Canada, there are likely to be pockets of success which can be identified and applied across the country.

What should consultation look like?

A recurring theme of the Forum, during the presentations and through the panel discussions, was the need for dialogue and discussion among stakeholders. But the nature of this discussion, and the context it should consider, were the subject of spirited views among some panellists. Should the patients have a direct voice? After all, they are the ones needing the biologics, and the ones affected directly by the safety and efficacy of SEBs. Which sort of patient would have a say, or be the focus of the consultation?

There are also ideas of consultation involving the broader public who pay taxes to support the high costs of biologics, and may face other unanticipated costs through SEBs? If there is a direct patient voice, what direct voice would be in place for taxpayers? While panellists did not share precise agreement on these matters, the importance of the LSAM forum offered as a platform for such discussion was noted.

RECOMMENDATION – CONTINUED CONSULTATION

As policy makers consider the issues, LSAM is well positioned to assist with a continued dialogue for development of policy in all of these areas – approvals, dispensing, financial support, post marketing surveillance. A consultation process involving LSAM would make an important positive contribution to discussion by policy makers touching on these key areas related to SEB policy:

- *What pricing and service model should be adopted to provide approved SEBs for patients in Manitoba?*
- *What post-marketing surveillance should be developed and maintained regarding SEBs to ensure patient safety?*
- *What lessons can be learned elsewhere, both in other provincial jurisdictions in Canada as well as within the United States and in Europe, as SEB policies continue to evolve?*
- *What sort of role should the voice of patients play, and how can that voice be added in a positive fashion to the development of SEB policy?*

Demand for SEBs is a reality in Canada, and the issue will continue to grow as more and more innovator biologics reach the end of their patents. Policy makers should **act now to prepare** for the increased use of SEBs and the implications on the public health care system. A constructive dialogue will be essential to these preparations. With the breadth of stakeholders LSAM is able to reach – all represented in the Subsequent Entry Biologics Forum - policy makers will be able to tap into the insights and knowledge of many critical stakeholders as they consider the opportunities and challenges of SEBs for Manitoba patients and their families.

i Conference Board of Canada: http://www.conferenceboard.ca/hcp/hot-topics/healthspending.aspx#top
ii Canadian Institute for Health Information – National Expenditure Trends, 1975 to 2014
iii ibid
iv Employment and Social Development Canada http://www4.hrsdc.gc.ca/.3ndic.1t.4r@-eng.jsp?iid=3
v Government of Manitoba, Estimates of Expenditure, 2015-16 Budget

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