

Launching a New Drug in Canada

Q & A for Entrant Companies



By Ravi Deshpande Pharm. D.

rdeshpande@phase4health.com



By Dale Weil

dale.weil@mckesson.ca

Development of pharmaceuticals by small research based organizations is increasing. Unlike multi-national firms, such companies need to find a strategy to develop the infrastructure and resources needed to launch a drug in Canada. Specifically, smaller organizations have the following challenges:

- ☞ The company infrastructure and expertise may be based on clinical knowledge and research rather than drug manufacturing, distribution and marketing.
- ☞ If based outside Canada, the company may not have operations outside the home country.
- ☞ The product may be a specialized one, with a small target group of physicians and patients; it may have advanced reimbursement and economic data requirements to obtain coverage.
- ☞ It may be the sole or even first product for the company.

While a detailed discussion of all the aspects of commercialization is beyond the scope of this article, a few relevant questions and answers are provided below.

LICENSE TO MARKET

Who approves drugs in Canada?

Health Canada, an agency of the Canadian

Federal government reviews New Drug Submissions (NDSs) and provides, upon approval, a Notice of Compliance (NOC) to market the product. Different types of NOCs correspond to restrictions on marketing that may be imposed.

What factors should a new entrant into Canada consider when submitting an NDS?

Companies without infrastructure in Canada need to establish a Canadian entity in order to file an NDS. For some drugs, there may be pressure to make the drug available prior to approval – Health Canada provides two ways to accomplish this, the Special Access Program (SAP) or through filing of a Clinical Trial Application (CTA), similar to filing a US IND.

DISTRIBUTION

What are the requirements to distribute pharmaceutical products in Canada?

A company must have a) an “establishment license” or b) a licensing or distribution agreement with an existing manufacturer or c) an “agency agreement” with a logistics provider who will carry out importation, quarantine and release on its behalf.

How will patients access the product?

If medication is to be used in an acute care setting, establishing a distribution network to hospitals is needed. If it is prescribed by physicians and requires general availability at retail pharmacies, it needs a broad distribution network. A more specialized medication with very small patient population and/or control on patient use may necessitate a customized distribution approach through a small number of specialized pharmacies.

What are the various distribution models available?

A pharmaceutical manufacturer can deliver directly to either hospital or retail pharmacies. In Canada almost 90% of the market is consolidated through the wholesale channel, whereby pharmacies enjoy a “one stop shop” benefit. In either case, a third party logistics provider or the manufacturer’s own logistics assets may be used to ship to wholesalers or directly to pharmacies. In the case of highly specialized, more restricted distribution models, a manufacturer may consider using an exclusive wholesaler and specialized pharmacy group.

How do I choose a distribution model?

A number of factors should be considered. Your infrastructure or planned infrastructure in Canada or licensing agreements will determine the need for a logistics provider. The therapeutic area and number of target patients, as well as specific requirements of your molecule will direct the choice of the best distribution model. Regulatory and other requirements for control of your product or its pricing are also important elements.

REIMBURSEMENT

Who Pays for Drugs In Canada?

Reimbursement of your product is perhaps the biggest single hurdle after you have received NOC. Canada has ten provinces which individually make decisions on whether your drug will be funded.

Continued on page 2

Launching a New Drug in Canada continued from page 1

In addition, numerous private payers (insurers, PBMs) will also individually decide whether to cover your drug. About 40% of all drug funding originates with provincial health ministries, while private drug plans cover about 40% of patients. Cash payers make up the rest.

How do I get my drug covered?

Canada has a highly developed system of review for products that seek public funding. The Common Drug Review (CDR) is a Federal agency, which reviews many new drugs and makes recommendations on whether a drug should be covered, but does not pay for any drugs—individual decisions to reimburse are left to each province. Depending on the drug, provincial drug plans or special provincial disease agencies (e.g. HIV, Cancer) require reimbursement submissions to make final funding decisions.

Private plans are similar to US private payers, but in general, Canadian private payers are less developed in their policies and restrictions.

Submissions must be made to each of these payers. A complete dossier which includes clinical, budget impact and economic data about your drug is required.

How long will coverage take?

Generally, public payers will not be reimbursing your drug for a period that can last up to 24 months. A period of at least 12 months should be expected.

PRICING

Will my price be controlled in Canada?

If you are selling a drug which is patented, or a generic drug which is covered by a provincial formulary, the answer is yes. In the former case, a pricing submission to the Patented Medicines Pricing Review Board (PMPRB) is needed. The submission will contain, among other things, a description of the clinical characteristics of the drug and its likely comparators (whether indicated for the condition or not). Eventual maximum allowed price will depend on how the drug is classified and possibly the price in markets outside Canada.

SALES AND MARKETING PLAN

Canada's 50,000+ physicians are comprised of fewer specialists and more family physicians than in the US. All physicians in Canada receive payments from their provincial government for providing services and cannot accept other payments for those services deemed medically necessary.

Marketing drugs, in particular specialty drugs, is a process of working with the small cohort of specialists who will influence and direct the use of your product. Physician practices have different incentives for performing procedures or providing infusions in comparison to the US. This may result in a different sales, marketing and distribution strategy for your product in Canada.

All the above questions highlight the complex nature of launching a new product in Canada. If you are launching in Canada for the first time, contact Ravi Deshpande at 800.811.9880 ext. 102 or rdeshpande@phase4health.com to discuss your strategy.

Specialty Products

New Products Dictate Consideration of Patient Treatment Pathways



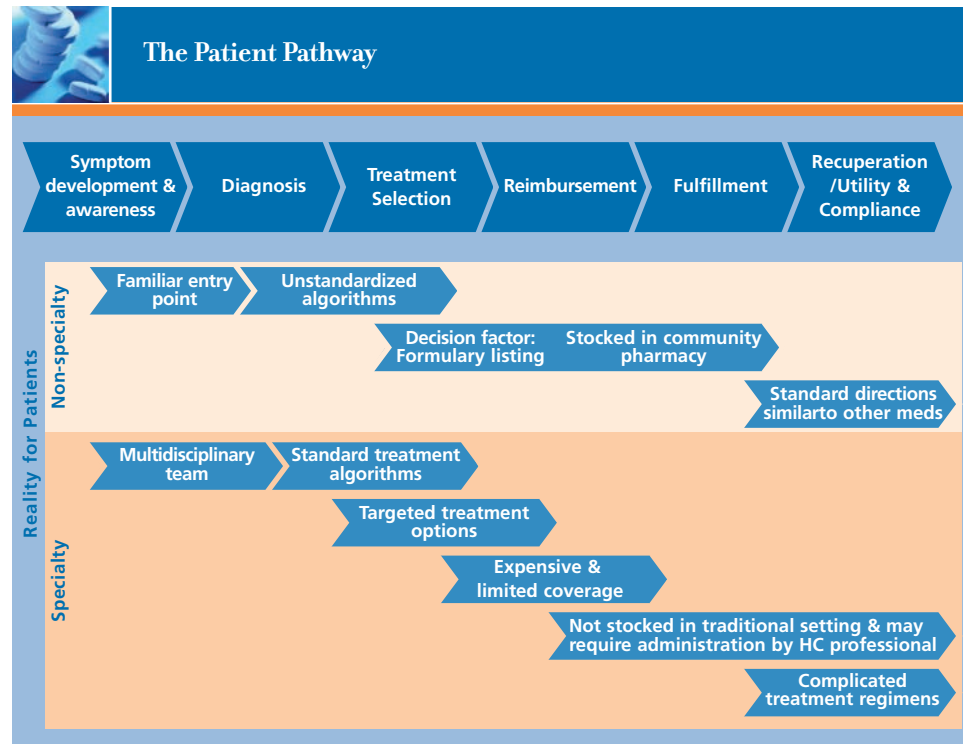
By Rose Fishman, BScPhm
rfishman@phase4health.com



By Jean Michel Coutu, R.Ph., MBA
jmcoutu@phase4health.com

As pharmaceutical companies continue to broaden their portfolios with specialty products*, the usual tried-and-true launch strategy of broadcasting key messages to physicians and patients is no longer sufficient.

Specialty products require a patient-centric, customized strategy to realize optimal market value. As the best-selling business strategy book "Blue Ocean Strategy" states: "Untapped value is often hidden in complementary products and services."



Providing a positive patient treatment experience

In the traditional marketing paradigm, the physician is top-of-mind and, patients often become the forgotten stakeholder. Because the patient treatment journey is considerably more complex for specialty drugs, it is essential to ensure patients' needs are met. They need the right support to ensure their access to and compliance with treatment.

The first step towards devising a strategy that provides optimum value to all stakeholders is to break down what is called the *patient pathway*. We define the *patient pathway* as the healthcare process for all patients from disease origination to treatment compliance. Naturally, every disease state and product will have a somewhat different *patient pathway*. However, a few activities are common as patients proceed from one phase to another. Consider the following questions, each of which illustrates a challenge for patients in a particular phase of the pathway. How do I get reimbursement for this product? Can my local community pharmacy dispense this? And, in the case of a drug requiring infusion or specialized administration: where do I get this product administered?

It is only once all the patient's product needs within disease state have been mapped out that a product strategy can be developed to leverage every touchpoint. In addition, this will uncover all the tangential considerations that will drive the strategy: distribution type, dispensing services, administration requirements, coordination of care, feedback to physicians, etc. These are all individual levers to optimize a patient-centric model.

Finding the right distribution model

As Anne Miao, Director of Business Development, discussed in her spring 2007 Catalyst article: "When a drug is used for a much smaller population, manufacturing production runs are proportionally fewer. On top of this challenge, the newer drugs are biotechnological molecules, usually with a shorter shelf life, less stability and difficult manufacturing processes. Smaller production runs also require tighter inventory management and control to ensure sufficient drug is available for



those who need it." Whether a cold chain, closed distribution network or a hybrid distribution model, a pedigree distribution model that controls the amount of inventory contained in the distribution pipeline, prevents any bull whip effect and feeds data back to product managers in real time. This is paramount for high-cost specialty products. Moreover, distribution no longer means a straight line from manufacturer to wholesaler to pharmacy or hospital. Product dispensing can also become a crucial value component in the drug distribution process.

Making specialists part of the product team

Pharmaceutical companies should look at physician specialists as an extension of the product team. Their input and endorsement can help craft an actionable and relevant product strategy. Knowing that patients are being well-managed through the *patient pathway* goes a long way to achieving a high degree of physician specialist loyalty. And to further increase prescriber confidence, it is essential to incorporate feedback loops so physicians have up-to-date information on the treatment progress of their patients.

Aligning with the sales force

Specialty sales forces need to understand all components of the product and service offering to be able to support physician specialists and ensure maximum patient enrollment. A focused understanding and continual review of the *patient pathway* is essential. With a thorough understanding of the *patient pathway*, the sales force can further assess the relevance of services, target adjustments required to improve patient and physician experience, and monitor the overall performance of the new strategy.

Going forward, a patient-centric game plan is required

In the past, specialty products have performed well because they were niche products in an environment with few competitors. Thus they were able to capture the attention of a select group of specialists.

As the market becomes increasingly competitive on multiple dimensions, this marketing strategy is no longer as simple as it once was. The success of specialty products now depends on a marketing strategy that aligns the four factors discussed above with the *patient pathway* as the keystone. In today's competitive arena, the most successful strategies will address the patients' experience and offer value beyond product utility.

Specialty products present unique marketing challenges. However, the over-riding principle is clear: an integrated approach, which facilitates the delivery of care throughout the continuum of the patient pathway, must be the central focus. When the overall marketing strategy provides a holistic, solution-based value proposition to patients, the loyalty of all stakeholders will follow.

* We define "specialty products" as pharmaceuticals that are high in value, may require special administration considerations, and/or require non-standard handling, storage and distribution.

For more information about Specialty Products, contact Jean Michel Coutu at 1.800.811.9880 ext. 423 jmcoutu@phase4health.com or Rose Fishman at 1.800.811.9880 ext. 104 rfishman@phase4health.com.

Risk Management — The Move to Implementation

Increasing Involvement by Regulators Means More Than Just Market Access



By Ravi Deshpande, Pharm. D.

rdeshpande@phase4health.com



By Paramjit Kaur, Pharm. D.

pkaur@phase4health.com

Talked about for decades, in the post-Vioxx® era pharmacovigilance activities have finally brought risk management to the forefront. Management of risk holds different meanings for regulators and drug manufacturers; however, in the end it is patient safety which is paramount.

The current system of drug regulation is a relatively recent phenomenon, dating from the 1950's in most western countries. The system has mainly been designed to perform the function of approving a molecule for sale and distribution, often as a one time event. Not much thought went into further monitoring outside of systems to collect voluntary spontaneous adverse event reports. The effectiveness of such a system has been crude at best, with catastrophic events required before any regulatory action was taken. In general this system of risk management, if the term "management" can even be used, contributed very little to the understanding of patient risk, both qualitatively (susceptibility factors, extent and duration of risk) and quantitatively (actual numerical data on risk versus benefit). Now, regulatory agencies are aggressively taking a greater interest in regulating an approved product throughout its life cycle, not simply authorizing its access into the market. This trend is global, hopefully fostering an environment of greater standardization and cooperation.

Regulating bodies worldwide are issuing guidance documents on pharmacovigilance, both internal and external policy statements on risk management, and using their regulatory muscle to enforce transparency in the activities and communications of a somewhat beleaguered pharmaceutical industry. By obligating pharmaceutical manufacturers to follow, in effect, regulators

are practicing organizational risk management by assuring their organizational goals of patient safety are satisfied. Furthermore, by removing the voluntary nature of these activities, the playing field has been leveled for pharmaceutical companies, reducing the somewhat perverse disincentives that exist in a spontaneous AE reporting system.

In the US, the Food and Drug Administration (FDA)'s Centre for Drug Evaluation and Research (CDER) has issued their *Guidance for Industry Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment* which outlines its strategies for the pre- and post-marketed product. Even though these are not legally enforceable, they do provide clear direction on signal detection, signal interpretation and pharmacovigilance plans. The FDA's risk management guidance incorporates risk assessment in the pre- and post-marketing scenarios, as well as risk minimization. Similarly, the European Union (EU) has forged even further ahead by mandating compliance and penalizing companies for non-compliance with EU regulations and not satisfying their obligations. *Guidelines on Pharmacovigilance for Medicinal Products for Human Use*¹ is an extensive document detailing specific mandated requirements for pharmacovigilance systems, monitoring of compliance, risk management systems, reporting, signal detection and communications activities. The European Medicines Agency (EMA) is responsible for "in particular by evaluation, coordination of the implementation of pharmacovigilance obligations and the monitoring of such implementation."² The EMA has a scientific committee, CHMP within which is the Pharmacovigilance Working Party (PhVWP). The PhVWP "is to provide advice on the safety of medicinal products and the investigation of adverse reactions, in order to enable effective risk identification, assessment and management, in the pre- and post-authorization phase."

Similarly, Health Canada (HC) has taken a stand. In an environment of increasing priority reviews and Notice of Compliance

with Conditions (NOC/c), Health Canada has plans to implement processes which monitor beyond the approval process. The number of NOC/c granted by Health Canada has increased over the past years from 4 each in 2004 and 2005, to 7 in 2006 and 3 in the first quarter of 2007 already. Most of these have been eligible for receiving an NOC/c because the molecules were indicated for oncology or other life saving conditions. With an NOC/c, Health Canada authorizes early market access of a promising drug, contingent upon the sponsor undertaking additional studies to support clinical benefit and enhanced post-market safety surveillance steps.

As such Health Canada's role has "been evolving from the traditional gatekeeper role of the past to include roles such as information provider and risk manager."³ With this evolution, Health Canada has reacted with the *Progressive Licensing Framework* (PLF), part of Health Canada's Blueprint for Renewal initiative which is an attempt to modernize the regulatory environment moving forward.

The foundation of the PLF is that knowledge and understanding of a drug occur over time and not at one point in time. The drug's safety profile is not completely known or available pre-market approval. The framework offers a three pronged methodology:

- 1 A life-cycle, evidence based approach** which will enable sound decision making on a scientific basis throughout the life cycle of the drug.
- 2 Good planning** which would enable "a proactive approach to managing both expected and unexpected issues".⁴ Pre-marketing filing with Health Canada will become more detailed with earlier involvement and evaluation of clinical trial methodologies, protocols, anticipated manufacturing changes and planning for post-market activities such as future studies, monitoring plans, surveillance strategies and risk management for the drug.

Continued on page 5

3 Accountability would rest with both Health Canada for licensing the drug and the drug manufacturer throughout the life cycle of the drug.

Internally at the organizational level, Health Canada has a strategy to implement an *Integrated Risk Management (IRM) Framework* to provide a “continuous, proactive and systematic process for understanding, managing and communicating risk from an organization-wide perspective”⁵ It has further developed a *Strategic Risk Communications Framework*⁶ to support its risk management processes.

Barriers exist to post marketing surveillance. Lack of awareness of processes, lack of commitment, quality of data submitted on reports have all been cited as challenges in drug safety monitoring in the post marketing environment. To combat these challenges, drugs with potential or identified safety risks have had risk management requirements mandated by regulators through various mechanisms such as post marketed registries. Examples include Revlimid® in the US and Iressa® in Canada, with more drugs in the pipeline which will have to satisfy stricter requirements for initial and continued availability in the respective market.

Yesterday, regulators made drugs available in the market. Today, regulators are following the drug beyond approval. There is a strong move towards greater engagement by regulators in the life cycle of drugs which means a shift towards an era of fostering collaborative partnerships between regulators and pharmaceutical manufacturers.

For more information about risk management, contact Ravi Deshpande at 1.800.811.9880 ext. 102 rdeshpande@phase4health.com or Paramjit Kaur at 1.800.811.9880 ext. 126 pkaur@phase4health.com.

¹ http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-9/pdf/vol9A_2007-01.pdf

² http://ec.europa.eu/enterprise/pharmaceuticals/eudralex/vol-9/pdf/vol9A_2007-01.pdf p16

³ http://www.hc-sc.gc.ca/dhp-mps/homologation-licensing/index_e.html Progressive Licensing Framework, Concept Paper for Discussion

⁴ http://www.hc-sc.gc.ca/dhp-mps/homologation-licensing/index_e.html Progressive Licensing Framework, Concept Paper for Discussion

⁵ Office of Integrated Risk Management. Strategy to Implement an Integrated Risk Management Framework in Health Canada. June 19, 2003.

⁶ www.riskcommunications.gc.ca Strategic Risk Communications Framework and Handbook for Health Canada and the Public Health Agency of Canada. November 2006, version 1, volume 1.

Drug Sampling: An Old Strategy Faces New Challenges



By Anne Miao, BScPhm, MBA
amiao@phase4health.com



By Sabrina El-Chibini, B.Sc. PT, MBA
sel-chibini@phase4health.com

Sampling drug products has been a traditional marketing tactic. Like coupons in the retail sector, sampling is sometimes a necessary evil and required to compete. However, in some circumstances, such as introduction of a new drug where sampling allows doctors to gain rapid use experience or where delays in therapy would lead to a lost script, it impacts positively on the ability of the pharmaceutical industry to gain market share and to maximize revenue while increasing adoption of therapy. However, sampling practices need to widen beyond the traditional approaches to allow higher degrees of control, and to prevent over sampling and cannibalization of sales. Following are factors that are influencing the evolution of sampling practices:

- ⌚ Heightened control required because of increased price or complexity of drug products.
- ⌚ Increasing importance of retail pharmacy in drug selection decision-making.
- ⌚ Market saturation and reduced physician availability.
- ⌚ Increasing need internally to demonstrate profitability associated with traditional sampling (as opposed to other marketing approaches).

Traditional sampling practices, (i.e. where sales representatives physically carry samples into physician offices) are aimed at leaving the drug in the hands of physicians while the information is fresh in their minds. Physicians also have an opportunity to gain experience in the short term to determine whether company claims are accurate. Sales representatives generally feel empowered by traditional sampling



Continued on page 6

techniques in that these improve access to physicians in addition to being powerful reminders of the messages they deliver. Traditional sampling, for these reasons, is commonplace largely for low cost, mass-marketed products.

Shortcomings of traditional sampling include the possibility of over saturating physicians and the lack of information on utilization. Traditional sampling is also the technique that provides the lowest level of control for the manufacturer.

Other more sophisticated physician sampling models are available that provide more control. In the "direct-to-practitioner" sampling model, physicians request samples from representatives, providing them with the necessary authorizations. Sales representatives in turn place an order that is shipped directly to the practitioners or patients. This model originated to address needs for specialty products (such as reducing the risks of sampling controlled substances) that require some control systems to be in place for the sampling process.

More recently and increasingly, innovative sampling techniques are being directed at retail pharmacy due in part to the recognition of the important role that pharmacists can play in affecting prescribing and patient therapy and outcomes. Pharmacists are also clinicians whom patients trust and seek out to gain information regarding medication. In sampling through retail pharmacy, manufacturers:

- ☞ use an existing community and "natural" channel,
- ☞ involve pharmacists; reinforce and optimize community pharmacists' role in patient education,

- ☞ inform pharmacists about new products, changes to existing products, new modes of administration, associated devices, etc.,
- ☞ sensitize pharmacists about product attributes and complementary service networks that are available to support patients, and
- ☞ deal with products that require cold chain, are controlled substances, are bulky or are otherwise unsuitable for sampling directly to physicians.

Controlled sampling at the level of retail pharmacy can be done by offering patients (via physicians with a prescription or at the pharmacy upon presentation of a prescription) a card or certificate with a unique identifier. These are pre-programmable and offer registered patients the opportunity to obtain a one-time sample product or device at the retail pharmacy of their choice.

Other card systems, also assigned on the basis of a unique identifier, allow more sophisticated programming and multiple use opportunities. These cards can be customized to any individual patient's needs to offer benefits and services for which a particular patient qualifies. This system allows sampling only once or at several points in time (same card) and can also couple sampling with additional integrated services such as reimbursement assistance or patient support while allowing fully automated features at the point-of-sale at pharmacy through habitual adjudication channels.

Single-use and multiple-use cards and redeemable certificates are patient-specific. The cards offer many advanced levels of controls as well as the potential for automation and reporting of administrative processes associated with these channels. These practices also eliminate the need to address the right amount of sampling as in traditional channels.

Even greater levels of control can be exerted by offering cards and certificates by order only, provided there are convenient channels through which these can be ordered. In the case of pharmacy, it is possible to couple ordering of cards through internet-based habitual ordering channels when pharmacists place their orders. Providing cards by order only facilitates the identification of interested niche markets which can help increase efficiencies in marketing efforts across the board for any given product. Sampling in this way can also be done for multiple products for any particular manufacturer, i.e. for a product portfolio and would result in the realization of cost-efficiencies as well as a branding opportunity.

Each level of added control is associated with specific service requirements, ranging from setting up an e-authorization and ordering system to the printing and programming of cards, to transactional fees, to administrative systems for reconciliation, to the integration of other value-added services, etc. Carefully designed sampling strategies that reallocates samples to the physicians that are more likely to prescribe and are receptive may yield a 14% profit increase over traditional sampling methods. These increases in benefits may be achieved without increasing the sample budget!

In summary, sampling does not need to be the traditional blunt strategy in today's marketplace.

For more information contact Anne Miao, BScPhm, MBA at 1-800-811-9880 ext. 135 amiao@phase4health.com or Sabrina El-Chibini, B.Sc. PT, MBA at 1-800-811-9880 ext. 128 sel-chibini@phase4health.com