

EUROPEAN GO-TO-MARKET PRIMER: WHAT YOU NEED TO KNOW BEFORE YOU LAUNCH

By Sabine Dettwiler

When launching a drug in Europe, manufacturers of pharmaceutical products will encounter a diverse array of markets and healthcare systems. A continent that comes third in terms of population size after Asia and Africa, Europe consists of 50 countries. Of these 50 countries, currently 28 are members of the European Union (EU). No common healthcare system exists across Europe; healthcare systems operate on a national level and are for the most part funded publicly.

Manufacturers introducing a brand into the EU region for the first time will find stark differences in the policies, preferences, and procedures they face from country to country from a regulatory, pricing and reimbursement, and marketing perspective. As a result, players in the space must be aware of local challenges well ahead of time.

To provide some perspective on the European market and help alleviate the threat of potentially brand-killing mistakes, this article will illuminate some of the unique factors manufacturers should bear in mind before attempting to commercialize a biopharmaceutical product in Europe for the first time.

Regulatory Environment

One common denominator of healthcare in Europe is the European Medicines Agency (EMA), a decentralized scientific agency composed of a network of experts across countries that evaluates medicines being developed for use in the European Union. The EMA serves a similar function to that of the US Food and Drug Administration (FDA) and provides a manufacturer with the possibility of a centralized procedure to get a drug approved. For European countries that



are not part of the European Union—non-member EU states—each of these have their own regulatory agency that manufacturers need to apply to on an individual basis in order to gain local marketing authorization.

In the EU, the maximum timeframe for the evaluation of a Marketing Authorization (MA) application is 210 days, excluding clock stops when additional written or oral information is to be provided by the applicant in response to questions asked by the Committee for Medicinal Products for Human Use (CHMP). If the CHMP accepts an applicant's request for Accelerated Assessment, then the timeframe for evaluation is reduced to 150 days, excluding clock stops. The justification for Accelerated Assessment needs to

address patients'unmet needs, the drug's major added value, and how the added value demonstrates that the drug represents major interest from a public health point of view. The ability to apply for orphan designation exists in the EU, however the application needs to be submitted to a different body: the Committee for Orphan Medicinal Products (COMP), which will review and grant approval for orphan drug status regardless of the CHMP review.

For pivotal trials, companies sometimes underestimate the need to design the trial with endpoints that are specific to an EU audience. The standard of care in any therapeutic category can differ between the US and the EU for example, and also

between the different countries within the EU; hence the comparator will need to be chosen accordingly. A trial comparing a drug against the standard of care in the US may not pass muster for European regulators. Hence, approved indications in the EU may differ from those for the same drug in the US even if submitted with the same trial data.

For example, the EMA has granted Novartis approval for the following indications for its drug Afinitor: breast cancer that is advanced and hormone-receptor-positive in women who have been through menopause; pancreatic neuroendocrine tumours; and advanced renal-cell carcinoma (RCC, a type of kidney cancer), when the cancer has worsened despite treatment with a VEGF-targeted medicine. Meanwhile, the FDA has approved Afinitor for treatment of postmenopausal women with advanced hormone receptor-positive, HER2-negative breast cancer; adults with progressive neuroendocrine tumors of pancreatic origin that is unresectable, locally advanced, or metastatic; adults with advanced RCC after failure of treatment with sunitinib or sorafenib; adults with renal angiomyolipoma and tuberous sclerosis complex (TSC); and adults and children 3 years of age or older with subependymal giant cell astrocytoma associated with TSC who require therapeutic intervention but are not candidates for curative surgical resection.

These product-label differences will add to the complexity of a launch for the marketing organization, because it will need to develop materials tailored specifically for European audiences down to the local level.

Once marketing authorization has been granted by the EMA, a manufacturer can market a medicine in the EU member states. However, due to the local reimbursement

system, most manufacturers will only officially launch once reimbursement of the drug has been approved by local authorities.

Pricing and Reimbursement

Clinical trial endpoints and comparators are also important with respect to reimbursement after regulatory approval. A varied field of data is required for each country's health technology assessment (HTA) process, which makes the tailoring of a global development strategy a real challenge.



In Europe, many diverging opinions exist in terms of what constitutes a drug's value and how it should be evaluated in the course of the HTA. Depending on the socioeconomic heritage, each market defines value differently. Switzerland, for example, with its free pricing and reimbursement, regards the drug price itself as a value indicator. Other markets like Turkey, the Netherlands, and Spain are driven by an overall budget impact perspective. Meanwhile, markets like Germany and the UK apply various cost-effectiveness angles to their definition of a drug's value.

In the EU, reimbursement timelines vary dramatically from country to country. This is important for companies when calculating cash flow, because even if the drug has been approved by the EMA, without country-level reimbursement approval, the companies will

not get paid for the product. In Germany, products are reimbursed immediately upon approval, whereas in Greece, it can take up to 18 months for pricing and reimbursement negotiations to be completed. France is among the countries in which the duration from EMA approval to commercialization can take between six to 12 months. In addition to reimbursement approval timelines, one must also consider that the budget holders for reimbursement are not necessarily the same as for national market access. In the UK, Spain, and Italy, regional or even local budget holders need to be contracted before any reimbursement can be granted and cash flow occurs. Hence, pharma companies

need to start engagement on these levels early, which requires on-the-ground resources and certain capabilities.

Key execution capabilities include value dossier assembly, medical writing, formulated

toolkit development, payer engagement modeling, and key account management. It takes years for manufacturers to develop these capabilities and for companies that are new to the business, it can be a challenge to develop them in-house. Partnerships or outsourcing may be necessary to compete.

The reference pricing system in the EU will need to be considered when setting the price for a drug, as it can have an impact on launch sequence and overall pricing and reimbursement strategy. In addition, differing prices among the countries can lead to challenges in the import/export of products between the markets. Similar to the US, which struggles with cheaper drug imports from Canada, Europe faces parallel imports across borders.

An important aspect to also consider when setting the price of the product and consequently its impact on forecasting

potential revenues is price evolution post launch, with drug prices generally decreasing in Europe year after year post-launch, while in the US drug prices may continue to increase annually post-launch.

Marketing

Europe is a very heterogeneous region. In order to develop a brand and product strategy, it is critical to understand the individual market environments. It starts with a brand name, which may have different meanings in local languages and, hence, may be inappropriate to use. A brand name needs to be found that can be used across various countries. This is becoming increasingly challenging with increasing numbers of drugs and more restrictive rules for name-giving.

Also, local preferences will need to be considered when choosing the administration of the drug. For example, while stakeholders in one country may prefer infusions, other European customers may prefer oral tablets. The tablets may then be packaged into bottles or blister packs again, depending on the preference of the country. Finally, labeling needs to be done in the local language.

Because healthcare systems vary from country to country, treatment decisions are made on different levels and include different stakeholders. Therapeutic areas such as lung cancer may be treated by pulmonologists in one country, and by oncologists in another country. As a result, it is crucial that local teams provide input to the overall positioning of the brand and customize messages to local needs.

Naturally, messages have to be in accordance with local laws and, again, be tailored to a local audience and market environment, as, for example, competitive products may vary across the different EU countries.

Conclusion

While this article only scratches the surface of the myriad complications and challenges inherent in bringing pharmaceutical products to market in Europe, manufacturers should not be discouraged from taking steps toward European commercialization. Making inroads into Europe represents a major opportunity for pharmaceutical marketers. According to the World Health Organization, spending on healthcare in some European countries makes up almost 11% of GDP,¹ and, after the US, Europe is the second largest pharmaceutical market in terms of sales.²

The diversity of European countries' regulatory, pricing and reimbursement, and marketing policies and procedures does create hurdles for marketers. But with proper planning and foresight, it is possible to clear those hurdles and achieve launch success.

¹ http://epp.eurostat.ec.europa.eu/statistics_explained/index.php/Healthcare_statistics#Healthcare_expenditure. Accessed 03/20/2014

² IMS Health Market Prognosis, June 2013

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