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Original Research

Time to Entry for Cancer New Medicines: From European Union–wide Marketing Authorization to Patients Access in Belgium, Estonia, Scotland, and Sweden

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ABSTRACT

Objectives: First, to quantify the median time from European Union (EU)-wide approval to first use (launch) for a sample of cancer medicines and number of launches in Belgium, Estonia, Scotland, and Sweden as of June 2015. Second, to assess whether longer times to launch or lack of launches affected medicines with high or low expected additional clinical benefit. Third, to identify possible determinants of the probability of a cancer medicine to be launched. **Methods:** Correlation between time to launch and a set of variables hypothesized to affect launch was tested using a complementary log-log model for a sample of 46 cancer medicines that obtained EU-wide marketing authorization between 2000 and 2014. **Results:** In median, for a sample of 24 cancer medicines that obtained marketing authorization between 2010 and 2014, the expected time from EU-wide marketing authorization to first use of a medicine was shortest in Sweden, 3.1 months, followed by Scotland (9.3 months), Belgium (14.8 months), and Estonia (27.8 months). Median times to launch were longer for the entire sample of 46 cancer medicines that obtained marketing authorization between 2000 and 2014. In the all-country model, medicines with shorter times to submission for reimbursement, local manufacturers headquarter (or local sales representative), and a Food and Drugs Administration priority review or a combination of expedited approval programs and medicines launched in Scotland and Sweden were associated with a higher hazard of launch. Longer times since EU-wide approval initially correlate with an increased hazard but as time further elapses they negatively affect the hazard of launch. **Conclusions:** Median times from marketing authorization to first use of cancer medicines were shorter for medicines launched between 2010 and 2014 versus sample-wide (2000–2014). In Estonia, more medicines than in the other countries were not yet launched at the end of the observation period. There was no correlation between Prescrire and European School of Medical Oncology Magnitude of Clinical Benefit Scale ratings of added clinical value and time to launch.

Keywords: access, cancer, medicines, survival analysis.

Introduction

The patient access to new medicines in Europe W.A.I.T. indicator shows that for medicines approved between 2011 and 2014, the median time from European Union (EU)-wide marketing authorization to patient access ranged from 42 days in Germany to 895 days in Lithuania [1]. Out of the 135 medicines within the scope of the analysis, 113 were available in Denmark versus 28 in Lithuania [1].

In the EU, a marketing authorization may be granted by the European Commission on the basis of scientific advice of the European Medicines Agency (EMA). This process, known as the centralized procedure, was introduced in 1995 and since 2004 it is compulsory for new cancer medicines not approved before May 20, 2004 [2]. It involves a single application, a single evaluation, and a single authorization throughout the EU [3]. Once an EU-wide marketing authorization has been granted, a medicine can in principle be marketed in every EU country and selected countries of the European Economic Area (Iceland, Liechtenstein, and Norway).

In practice, patient access to new prescription medicines, particularly costly ones, will be severely limited if the medicine is not covered by the publicly funded health care system. Manufacturers will therefore generally make a reimbursement application to the national competent authorities of the countries in which they intend to market their medicines. Given that pricing and reimbursement is a national competence, processes and requirements vary across the EU. The overall time frame within which pricing and reimbursement procedures should be completed however is set by the European Commission in the Transparency Directive to 180 days for innovative products and 90 days for generic products [4].

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Table 1 – Literature review on time to launch of new medicines.

Medicines included	Time period and geographical coverage	Findings	Reference
85 new chemical entities covering different therapeutic areas	Launches between 1994 and 1998 in the outpatient sector in 25 countries	Only 55% of the potential launches occur. The United States experienced the highest number of launches (n = 73) and a mean lag of 4.2 mo, whereas Japan experienced the lowest number of launches (n = 12) with a mean lag of 23.5 mo. After controlling for a number of variables, the study finds that expected prices or market size affect both the number of launches and the time to launch	Danzon et al. [31]
1482 unique molecules covering different therapeutic areas	Launches between 1980 and 2000 in G7 nations (United States, Japan, Germany, France, Italy, the United Kingdom, and Canada)	Market characteristics alone correctly predict entry for only about 30% of the sample. Including firm's characteristics however improves this prediction substantially. A new chemical entity is 1.5 times more likely to be launched in markets that share a border or a language of a manufacturer's country of headquarters	Kyle [10]
1444 new chemical or molecules entities	Launches between 1980 and 2000 in 28 countries (21 of which were OCED members at the time the study was conducted)	This study confirms the influence of price regulations on launch patterns in the country imposing them and beyond	Kyle [9]
836 new pharmaceuticals	Launches between 1982 and 2002 in 68 countries at all income levels	Only 20%–50% of all drugs launched globally were on the market in any country after 10 y. The percentage was 60%–85% for high-revenue blockbuster medicines. Price regulation and intellectual property rights were found to affect launch times	Lanjouw [15]
642 new chemical entities covering different therapeutic areas	Launches between 1983 and 2002 in up to 76 countries at all income levels	Only 41% of the total products were launched in more than 25 countries. Price regulation was found to delay entry, whereas more extensive patent protection, health policy institutions, and economic and demographic factors were found to reduce time to entry	Cockburn et al. [16]
22,397 new chemical entities	Launches between 1999 and 2008 in 20 countries (major OECD markets plus South Africa)	This study finds that price regulation, market size, and regulation affect launch times of new medicines. Their effect is however counteracted by firm's economies of scale, the therapeutic importance of specific product innovations, and market size	Costa-Font et al. [11]
New molecular entities (sample size not stated)	New molecular entities that obtained marketing authorization between 2009 and 2013 across 18 developed countries	Large variation in time to launch (90–430 d) and time to reimbursement from launch (90–540 d) among 18 developed countries was found in this study. Countries were classified into three groups: fast launch and reimbursement, fast launch but slow reimbursement, slow launch but fast reimbursement after launch. In countries with slow launch,	Hickson et al. [33]

continued on next page