

Exploring the Value of Pharmaceutical Investment

As governments across the world continue to pour billions into the financial markets to help prevent a global depression, the budgetary pressure on traditional government services will become even greater. This will be particularly true for healthcare, already top of mind for governments and their citizens. Across markets, regardless of their respective methods of healthcare financing, the pharmaceutical industry faces continued scrutiny over its pricing. A clearly earmarked drug spend is an easy target when reviewing healthcare expenditures and is much less politically sensitive than doctors' pay or the amount spent to remedy medical errors. To prepare for the ever mounting pressure to reduce drug prices, industry and healthcare funders alike should ask: what is the true value of pharmaceuticals, and is this a sound investment?

The British Return on Investment

The UK market is one of the most aggressive in defining value thanks to the activity of the National Institute for Health and Clinical Excellence (NICE). The UK's Office of Fair Trade further pressed the value of pharmaceuticals question in its 2007 report. Given this focus on drug value and well reported public data from the Department of Health and OECD, the UK's National Health Service (NHS) can be used as a starting point to review pharmaceuticals as a healthcare investment and question if that investment should continue.ⁱ

To put forward an unbiased review of England's investment in pharmaceuticals, this article looks at three out of the top five therapeutic classes as defined by 2007 global pharmaceutical sales.ⁱⁱ Recognizing that other factors in addition to drug utilization are at play, a comparison of spend over a ten year period in England against changes in both health and quality of life outcomes highlights that pharmaceuticals are a high-return investment that has greatly benefited not only the healthcare system in terms of reduced costs but also – and even more so – patients.



UK drug spend as a percentage of total healthcare expenditure in 2007

- Drug spend 10.3%
- Other health expenditure

Oncology

Perhaps one of the most emotive disease areas, cancer is likely the most publically debated. Despite being the disease state with the highest global spend, total expenditures in England on cancer drugs are less than other therapy classes such as cardiovascular disease and respiratory disease. NICE has developed over 60 appraisals on cancer, more than in any other disease area. However, the Department of Health is becoming more sympathetic to patients. In response to very public campaigns, the Minister of Health lifted the ban on top-up treatments on 4 November 2008. Previously, patients who paid out of pocket for any non-NICE approved drug were forced to pay for their entire treatment, even for services traditionally provided by the NHS such as chemotherapy.

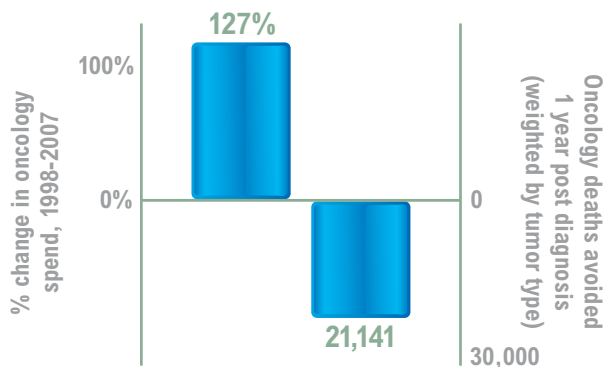
This focus on and effort to control cancer spend are warranted, but the metrics applied are questionable. The total cost of all cancer drugs prescribed in England increased by 127% (£144.6 million in 1998 to £328.2 million in 2007). This rise in spending is a direct result of the significant investment by the pharmaceutical industry to bring new drugs to the market such as Herceptin and Eloxatin in 2000 and Glivec in 2001. However, other treatments, such as Avastin, which is indicated for use in a number of solid tumors, and targeted kidney cancer therapies including Nexavar, Sutent, and Torisel are generally not funded by PCTs. Given all this, is investment in oncologics prudent?

Patients (and patient groups) say yes. The research and development investment into oncology over the past decade has enabled patients to live longer and better-quality lives. For example, one-year survival rates in England and Wales increased by a weighted average of 2.9% between 1996-1999 and 2000-2001. In other words, more than 21,000 additional patients were alive after one year following diagnosis and treatment. Herceptin can lead to increases of 33% in overall survival and a 50% gain in disease-free survival for breast cancer patients. Even higher results were found for Glivec, a drug for chronic myelogenous leukemia (CML). A New England Journal of Medicine article describes overall survival found to be 95% after excluding causes of death unrelated to CML or prior bone marrow transplantation.ⁱⁱⁱ Meanwhile, the kidney cancer drugs that have been blocked by NICE have demonstrated a potential to increase overall survival by five to six months longer than comparators.

Many may rightly say that the majority of new and high-cost cancer therapies have not cured cancer and only prolong life

for a short time. However, this end-of-life period has very high value for many patients, and reductions in mortality rates for patients and shortened average hospital stays should not be dismissed. For example, a study shows that colorectal cancer patients receiving treatment with Xeloda as compared to the previous standard of care not only had improvements in disease free survival and overall survival, but also had fewer hospitalizations and medications that contributed to a cost savings of £3700 per patient for the NHS.^{iv}

Cost and Benefits of Oncologics



Meanwhile, other cancer therapies work to improve quality of life but have no direct impact on the cancer itself. For example, anti-nausea drugs in the NK-1 class such as Emend make chemotherapy more manageable for high-need patients, thereby improving the likelihood of success of the primary therapy. Should supportive care be valued less than improvements in mortality? While NICE has not yet reviewed Emend, the Scottish Medicines Consortium has recommended restricted use which suggests that the SMC and those PCTs who follow its guidance are at least recognizing its value in the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based chemotherapy.

Cancer drugs are costly but valuable, and patient access has traditionally been restricted due to the £30,000 cost per QALY threshold informally imposed by NICE. Without such restriction – based on a figure developed years ago and now applied across all disease states – more value could have been provided to patients who likely place a high premium on additional months of life. In addition, due to the great need for new therapies in oncology, many treatments are studied first in late-stage patients where they may not demonstrate their full long-term potential (e.g., Herceptin has shown significant value in progressively earlier-stage patients in the years since it launched). Perhaps because of significant public scrutiny, the NHS agrees that cancer is a special case and has warmed to the idea of increasing the QALY threshold for

cancer. The Minister of Health announced earlier this month that the NICE ceiling may be adjusted up to £80,000 a year.

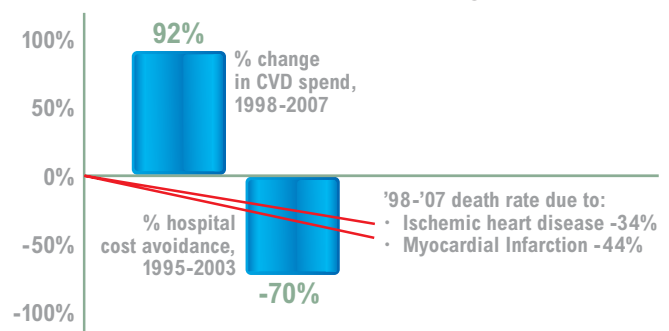
Cardiovascular disease

Closely following oncologics, lipid regulators account for over 5% of global sales. It is also an important therapeutic class for healthcare providers as lipid regulators are the primary combatant against cardiovascular disease (CVD), a leading cause of death. From 1998 to 2007, the amount spent on drugs treating CVD increased in England by 93% (from £940.3 million to £1,813.4 million). This trend was fueled by the launches of blockbusters such as Lipitor in 1997 and Plavix in 1998. Although this was a significant investment, the fundamental question is whether patients and the NHS benefited from this allocation of resources.

In the past decade, the death rates for ischemic heart disease and myocardial infarction in the UK declined by 34% and 44% respectively. Although a decline in national smoking levels also would have contributed to this trend, studies find that pharmaceuticals such as Plavix, ACE inhibitors and statins lead to lower mortality. These positive changes further translate into financial savings for society, especially when considering the production losses from cardiovascular deaths.

Health and societal benefits have been shown to be direct consequences of greater investment in appropriate pharmaceutical utilization. A study based on twenty OECD countries from 1995 to 2003 finds that countries that invested more in cardiovascular drugs had consequently larger reductions in hospitalizations and mortality due to CVD. By not investing in cardiovascular drugs, per capita hospitalization costs in these countries would have been an astounding 70% higher in 2004.^v

Cost and Benefits of CVD Agents



While the case for cardiovascular drug budgets appears very well justified in both healthcare and societal terms, it is also important to note the amount spent on CVD globally has fallen in 2007 by almost 7%. This fall in spend is due to expiration of patents such as Lipostat in 2004 and Zocor in

2006. These agents therefore still represent a valuable investment with an even higher rate of return, but it will be important for the NHS to continue to support new branded agents that offer incremental value in the management of CVD, and not merely to rest on the laurels of the pharmaceutical industry's past drug development success.

Diabetes

While only the fifth largest therapeutic class globally, pharmaceutical management of diabetes is growing worldwide and England has invested heavily in this disease area. Total expenditures on antidiabetic drugs increased by 256% (£167.0 million in 1998 to £594.1 million in 2007). It is easy to associate the dramatic increase in spending on new drugs such as long-acting insulins (Lantus and Levemir), as well as Actos and Avandia in the TZD class. It must also be noted that the patient population has increased by approximately 80% over the same time period and that the use of combination treatment regimens as standard of care has increased.^{vi}

Looking beyond surrogate endpoints such as HbA_{1c} reduction, antidiabetic agents have been successful in controlling and managing this disease. The average length of inpatient stay due to diabetes declined by 19%, and the number of emergency visits and admissions as a percent of patient population declined by 31% and 47% respectively. This substantial decline in hospitalization allows hospitals to shift resources elsewhere, effectively filling budget gaps from the savings created by better management of diabetes.

Conclusion

The focus on the cost of pharmaceuticals continues unabated, but relatively less attention is given to the value they have delivered to individuals, the healthcare system, and all of society over a period of many years. Based on this review, and despite the recognition that many factors can affect the real health outcomes discussed here, investing in pharmaceutical therapy clearly does deliver strong clinical and economic benefits. In this context it is fair to change the familiar question targeting innovative drug manufactures from "should the money spent on drugs be reduced or reallocated?" to "should drug budgets be increased?"

Over the past decade, there have been simultaneous and positive correlations in England between expenditures on pharmaceuticals in high-burden disease areas such as cancer, CVD and diabetes, and important clinical and resource utilization metrics in the same disease states. With the support of objective and rational evaluations such as this, the pharmaceutical industry can seek to shift the debate from

overly generalized and ill-informed attempts to curb pharmaceutical budgets and utilization, to widening access to appropriate pharmacotherapy as determined by metrics and outcomes most relevant to each disease state. While the Department of Health and the Association of British Pharmaceutical Industry hammer out the remaining "value" negotiations regarding the Pharmaceutical Price Regulation Scheme (PPRS), it will be to the advantage of both industry and government to take a lesson from the financial markets and to examine real risk-reward profiles prior to allocating finite investment resources.

- i Cost data is from the Prescription Cost Analysis (Department of Health). Hospitalization statistics are from the Hospital Episode Statistics (Department of Health). Mortality statistics are from OECD Health data 2008.
- ii Top-line Industry Data: 2007 Global Sales and Prescription Information (2008). <http://www.imshealth.com>
- iii Kantarjian et al (2002). Hematologic and Cytogenetic Responses to Imatinib Mesylate in Chronic Myelogenous Leukemia. *New England Journal of Medicine*. Vol 346 (No 24): 645 – 652
- iv Cassidy, J et al. (2006). Pharmacoeconomic analysis of adjuvant oral capecitabine vs intravenous 5-FU/LV in Dukes' C colon cancer: the X-ACT trial. *British Journal of Cancer*. Vol 94 (No 8): 1122 - 1129.
- v Litchenberg, F. R. (2008). Have newer cardiovascular drugs reduced hospitalization? Evidence from longitudinal country-level data on 20 OECD 1995 – 2003. National Bureau of Economic Research.
- vi Joint Health Surveys Unit (2008). Cardiovascular disease and risk factors. Health Survey for England 2006. The Information Center.

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