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GAO extraordinary drug price increase report – a red herring?

The US Government Accountability Office (GAO) in January of this year released a new report analyzing brand name prescription drugs with “extraordinary price increases” over the period 2000 to 2008.¹ An extraordinary price increase was defined as a one-time increase of 100% or more.

A closer look at the GAO analysis reveals the price actions taken by “brand manufacturers” are exceptions rather than the rule. The primary drivers to the price increases identified by the GAO can be attributed to the inclusion of repackaged drugs and drugs which face patent expiration.

A half analysis

The GAO report’s primary conclusion is that “lack of therapeutically equivalent drugs and limited competition may contribute to extraordinary price increases”. While these are two principal conditions supporting price flexibility, this report can easily be misinterpreted as evidence that the branded drug industry engages in price gouging of its customers – both payers and patients.

The GAO report notes that “limited availability of therapeutically similar products may be due to patent and market exclusivity protections that block competitors from making similar drugs,” thereby suggesting that some companies can raise prices at will. This ignores the notion that rational marketers price new products from the point of

market introduction at prices that reflect value and maximize profitability. Most drugs compete with many other non-therapeutically equivalent products in their markets, thereby creating a value-based competitive price ceiling that typically prevents significant price increases. It is around this component that the report may serve as an unfortunate distraction from the many valid arguments as to why novel biologics deserve reasonable market exclusivity and data protections.

The GAO analysis appropriately cautions that the drug products identified in the study account for less than one percent of all branded products on the market, and that more than half of the 416 brands with extraordinary increases were price actions taken by repackagers, not the original manufacturer. Repackaging is a very small, distinct area of health care delivery where third parties (physicians, clinics and even health maintenance organizations) acquire drugs from the original manufacturers for distribution in more patient-appropriate packaging. Repackaged product typically accounts for only a small fraction of a given brand’s total sales. Because of this value-add effort in the supply chain, repackagers can achieve much higher prices than the originator national drug code (NDCs). In California, repackaged drug reimbursement rates can be 200-300% higher than traditional channel prices.² The report does not specifically address the volume of package sizes on which price actions were taken, nor does it mention changes in volume that could have resulted from price increases.

For those searching for a price-gouging smoking gun, the price actions by the manufacturers, not the repackagers, would be the ideal target. However, a review of the brand name products on the manufacturer list reveals brands that are primarily older products that had lost, or were close to losing market exclusivity at the time of price action. In addition, some brands, while beyond exclusivity, do not have generic competition as their market shares and potential are very low, and they may be targeting orphan uses. Some of these products have been acquired by “specialty” pharmaceutical companies that acquire older, underfunded brands from larger companies and then reposition them for more targeted market opportunities that arguably may be more valuable to the healthcare system.

Role of the Market

An important market dynamic absent from the report are payer reactions to such extraordinary price actions. Essentially three basic groups pay for prescription medicines in the US – public/government bodies like

Medicare and Medicaid, private insurance companies, and patients themselves in the form of managed care cost-sharing policies or fully out-of-pocket for the uninsured.

The US government is no doubt a significant payer for the products identified in this report and it has built-in policies to control the cost impact of such actions. Medicaid, which covers drug costs for poor and disabled, can account for 15% or more of a product's customer mix. Drug manufacturers cannot raise their Medicaid prices at a rate higher than the consumer price index (CPI) (if they do, they must provide supplemental rebates to Medicaid). For these brands, price increases can be a zero sum game.

Private payers (employer funded and Medicare Part D) most likely cover the majority of the patients who use the branded drugs in this report, and one must remember that they negotiate actual prices paid in return for access privileges. Actual net price paid is often well below catalog list price level for many brands within highly organized managed care plans and pharmaceutical benefit managers. Additionally, private managed care payers can employ a variety of protections and reactions to price increases deemed excessive and beyond normal value-based pricing levels, such as capping clauses. For private plans without such protections, they can react by moving brands to higher copay tiers, taking brands off formulary entirely, or adding stringent restrictions on provider use such as step protocols and prior authorization requirements. The very threat of these responses typically prevents brand manufacturers from pushing the envelope of price increase policy.

A More Rigorous Analysis

A study with more teeth would focus on price increases of market-leading innovator brands that account for the majority of health spend on drugs. Here they would certainly find many price increases close to the CPI increase, as many large-selling brands must avoid the incremental rebate penalties when they have meaningful Medicaid market share, or are limited by Medicare Part B reimbursement constraints. Such a study would also find brands with increases regularly exceeding 15% annually, but once again it is likely they would conclude these are driven by many of the rational market factors mentioned above, not by unconstrained price freedoms afforded by patent laws. Managed care payers typically begin to take note of price increases that exceed 10-15% and if they defy competitive and value-based market dynamics, they will react with access restrictions that will surely reduce share and demand. Novel biologics in orphan-like disease categories today are known to have larger average annual price increases than traditional small molecule agents that compete in broad market indications.

Payers often tolerate these price increases where the products are well differentiated and offer good value in specialized disease areas with high medical need.

Multiple sclerosis provides an illustration, as a billion dollar category in which 2 of the 4 leading biologics in the category – Copaxone and Rebif – have been increasing price by over 20% annually for the last three years. Their patents are expiring in the next few years, but it is also likely that payers still see evolving and growing value in these agents' potential to modify the course of MS, a disease that leads to major disability in patients. Given relatively similar perceptions of safety and efficacy, the four major disease-modifying MS biologics are now competing on net price through contracts. Select payers may tolerate the 20%+ increases if their contracts contain price cap clauses requiring additional rebates for price increases exceeding a defined level.

In response to a New York Times article late last year suggesting that drug manufacturers may be artificially raising prices in anticipation of new reforms, four members of Congress requested that the GAO conduct yet another analysis of drug industry price increase policies. This time the requested analysis will explore more than just "extraordinary" increases, looking at recent trends for widely used brands and examining drug makers who exhibit anomalous drug pricing trends in the time leading up to potential pricing constraints associate with healthcare reform. In the letter to the GAO, the representatives state that "any price gouging is unacceptable, but anticipatory price gouging is especially offensive".

Be Prepared

Ironically, these GAO drug pricing reports provide industry an opportunity to remind policy makers that patent protections are not a license to raise prices at will, that all products must work within the rationale parameters of value-based pricing and market competition. Should the health reform bills in their current forms die as expected, Congress is likely to retrench to a few key bipartisan issues (Medicare Part D donut hole, biosimilar legislation and hospital costs), and they are almost certain to go back to the drawing board on data exclusivity for biologics, and reports like this will only complicate new negotiations between industry and the federal government. Based on this, drug industry groups like PhRMA and BIO may have to retool their arguments in defense of industry pricing policies, which must also include price increase/action strategies.

1. United States Government Accountability Office (December 2009). Brand-Name Prescription Drug Pricing: Lack of Therapeutically Equivalent Drugs and Limited Competition May Contribute to Extraordinary Price Increases. Report to Congressional Requesters. GAO-10-201.

2. Wynn, Barbara O. (2005). Paying for Repackaged Drugs Under the California Workers' Compensation Official Medical Fee Schedule. WR260-1. Rand Corporation.

Mind the Gap

Assessing the different data requirements between HTA and market access bodies

Four years in the making, the developments of the European Network for Health Technology Assessment (EUnetHTA) were presented last fall at the Drug Information Association HTA Forum in Paris, France. An initiative that intends to inform various healthcare stakeholders on the clinical, economical, social and ethical aspects of health technology, EUnetHTA aims to harmonize the HTA evaluation process across Europe.

The EUnetHTA has several activities in operation. With funding from the European Commission, the network is launching their next activity, the Joint Action on HTA 2010-2012. This involves 33 organisations from 23 EU Member States, as well as 19 organisations from 9 European collaborating partner countries. These stakeholders, which include HTA divisions of ministries of health, medicines agencies, and healthcare administrations, will work together to implement a European HTA collaboration.

The Joint Action on HTA aims to refine assessment methodology and develop tools to be used locally, regionally within a country and nationally across Europe. As its Director of Secretariat, Finn Børlum Kristensen stated at a HTA conference in London in December 2009, that while the Joint Action on HTA's purpose is "not to dictate" HTA in the different EU member states, it "may influence it."

Whether or not this evolves into a centralised EU HTA process will depend on EU Member States' willingness to relinquish any of their authority over health care decisions, which Member States have been reluctant to do to date, as evidenced by the European Council's failure to reach a common position on the cross-border health care directive at the end of 2009. While the countries debate how to move forward with this initiative, the pharmaceutical industry needs to be active in influencing both the appropriate role of HTA and realistic expectations for data requirements to help ensure access to new medicines across Europe.

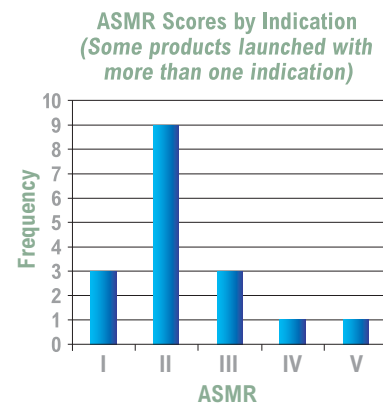
Market Access Inequalities

Unequal access to pharmaceuticals exist because European HTA and market access bodies are requesting more and often different levels of clinical evidence than regulatory authorities before allowing drugs post-market authorisation. By looking at twelve European Medicines Agency (EMA) approved oncology drugs and their assessments by the French Transparency Commission (TC) and UK National Institute for Health and Clinical Excellence (NICE) – which have very different methods of therapy assessment, we can

see how different data expectations have lead to disparity in terms of access between these two European markets.

France Driven By Clinical Benefit

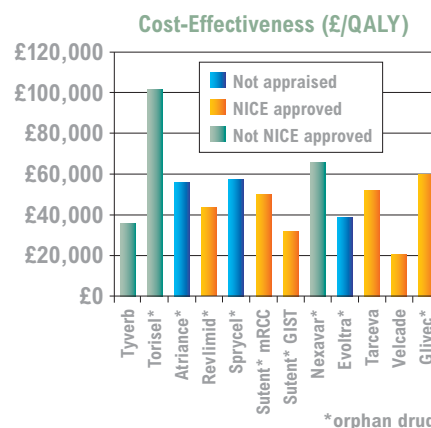
In France, drugs are assessed based on innovation over the standard of care and are assigned an *amélioration du service*



médical rendu (ASMR) score from I to VI, where I is considered a breakthrough therapy. The majority of the oncology agents reviewed were awarded an ASMR score of II, indicating substantial improvement over existing treatments. As it is often the case, manufacturers are required to submit post-market authorisation clinical studies. For example, the TC recommended Velcade for reimbursement but required the manufacturer to conduct a follow-up study. If the improved health benefit is not considered significant enough, the Transparency Commission will not recommend reimbursement. For example, Tarceva's metastatic pancreatic cancer indication was not recommended for reimbursement due to insufficient evidence of health gain over its comparator (Gemzar).

Cost-Effectiveness in the UK

In contrast to the TC, NICE uses cost-effectiveness to try to ensure value for money and equality in funding across the



UK. In general, interventions with a cost per QALY above NICE's £30,000 threshold face the risk of negative guidance, but the threshold may be more flexible for oncologics. Those approved had a cost per QALY of £60,000 or lower and were generally orphan drugs (4 out of the 5 NICE approved). To avoid negative guidance (which significantly reduces access), some manufacturers have engaged in risk-sharing agreements with the payer to lower their drug's cost per QALY. Revlimid, Sutent, Tarceva and Velcade were positively appraised because the manufacturers agreed to provide free goods.

| Market Access Body | Recommended for Reimbursement | Not Recommended for Reimbursement | Not Evaluated |
|--------------------|---|---|---|
| France TC | <ul style="list-style-type: none"> · All drug indications except Tarceva for metastatic pancreatic cancer | <ul style="list-style-type: none"> · Tarceva (metastatic pancreatic cancer) | |
| UK NICE | <ul style="list-style-type: none"> · Revlimid · Sutent · Tarceva (NSCLC only) · Velcade · Glivec | <ul style="list-style-type: none"> · Torisel · Nexavar · Tyverb (interim decision) | <ul style="list-style-type: none"> · Tasigna · Atriance (SMC ✓) · Sprycel (SMC ✓/ AWMSG x) · Evoltra (SMC ✓/ AWMSG ✓) |

New oncology drugs are normally introduced last line in populations where life expectancy is typically short. While a modest gain in overall survival (~3 months) is highly valued by the TC, a 3 month survival gain does translate into a substantial benefit in terms of a QALY gain. It is these differences in assessing that contribute to access inequality between the two countries.

Different methods of assessing value also impact drug spend and survival. According to IMS data, France spends €32 per capita on oncology drugs, while the UK spends €12. According to Graeme Poston, UK cancer specialist, France spends €8.14 per capita on breakthrough cancer drugs, while the UK spends €0.66. This disproportional spending contributes to differences in outcomes between the two markets. The EURO CARE working group found that the five year relative cancer survival in France was 56.6% for women and 45.5% for men, compared to 51.4% for women and 41.4% for men in the UK.

Improving Access

To increase access to oncology medicines, various initiatives have been put in place by the French and British governments. France introduced the Cancer Plan which prioritises equity of access to oncology care. In the UK, policies to improve access to innovative drugs and help refine the UK's HTA methodology include the Cancer Plan,

Cancer Reform Strategy, End of Life Guidance and Innovation Pass Scheme, but their impact is yet to be seen.

These access programmes, along with the different drug assessment methodologies in France and the UK, have contributed to different degrees of patient access in their respective countries. In France, virtually all of the oncologics were granted market access, contributing to good survival rates that are improving. In the UK, about half of the oncologics were approved, contributing to poorer health outcomes that are not improving.

If improving the UK's record of treating oncology is a measure of NICE's success, then NICE needs to continue to review what is an appropriate level of spend. However, payers and manufacturers need to reassess their oncology expectations. While an oncologic may provide a small incremental benefit to existing treatments, patients may see this as an important benefit.

Conclusion

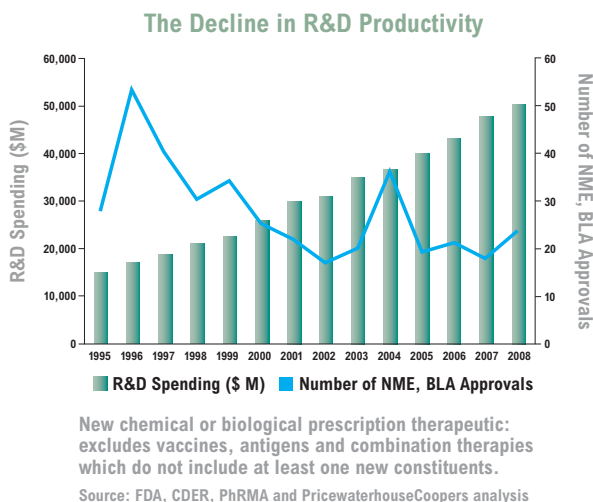
The EUnetHTA Collaboration intends to streamline payer expectations and benefit industry by creating a 'core' set of data requirements. While many will debate whether or not there should be a uniform approach to HTA assessment across Europe – at least in terms of data requirements – the important, first step is to understand the strengths and weaknesses of current HTAs. Further, those involved in the EUnetHTA should be wary of the data requirement differences of various market access bodies and of their intended and unintended consequences on patient access and health.

While the EUnetHTA continues to move forward, market access bodies and industry should continue to work together to devise a system or systems that most appropriately balances data needs against patient needs. At both the member state level and with the EUnetHTA, industry needs to stay engaged in conversation with payers regarding what type of clinical data will be required for market access and how feasible it is to provide.

To be able to assess the potential impact of EUnet HTA, industry also needs to understand how the evidence base they are creating will be applied in each market. Moreover, industry should have a contingency plan in anticipation of a greater number of HTA and market access bodies expecting additional data, such as resource utilisation. Companies should compare the supplementary economic or outcomes data required with the evidence they are currently submitting post-market authorisation and incorporate the expense for obtaining this extra data into development costs.

Business Development and Pricing and Reimbursement: An Integrated Approach to License Evaluations

The pharmaceutical industry is undergoing a paradigm shift that is altering the traditional drug development pathway. Many of the largest “blockbuster” drugs are scheduled to go off patent in the next few years. The pharmaceutical pipelines that many companies have relied on to replace earnings for drugs going off-patent are alarmingly thin. The decreased R&D productivity in the pharmaceutical industry is leading companies to increase their reliance on external partnerships in order to fill some of those gaps.



The task of evaluating potential partnerships and licensing deals generally falls upon the business development (BD) team. To properly assess a potential partnership, the BD team must understand and evaluate a variety of metrics including the intellectual property, commercial value of the product, synergy with the current pipeline, and potential legal issues. In many instances, unfamiliarity with the therapy area, market conditions, and competitive landscape leads to generalizations and assumptions based on unproven ‘rules of thumb’. As a result, teams face the possibility of inaccurately estimating the product value, missing critical development opportunities, or market challenges.

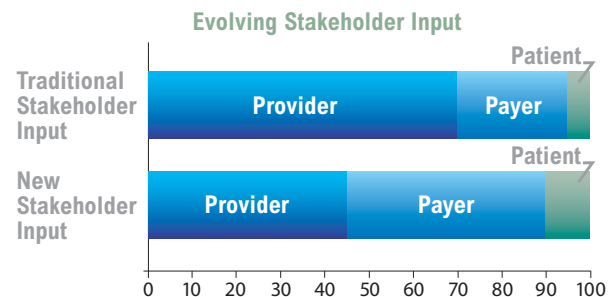
Pricing and Reimbursement (P&R) Departments: Underutilized Commercial Assessment Experts

The dynamic nature of the healthcare environment creates challenges and opportunities that must be considered

when evaluating a product or therapeutic area. In this environment, product viability and success is largely dependent on understanding the product’s potential to demonstrate clear therapeutic improvement versus alternatives, which then must be translated into favorable pricing and market access.

John Hall, M.D., VP product development at Quintiles, said that “around 14% of drugs fail to get to market not because of safety or effectiveness but for strategic reasons. To my mind this means pharma are still not involving their commercial people early enough in the clinical development.” 2006

In many instances, BD teams are unfamiliar with the market fundamentals (e.g., payer coverage and reimbursement policies) and trends (e.g., increasing patient out-of-pocket burdens). Familiarity with both are essential to properly assess the commercial potential of a product, especially in light of payers’ increasing influence over a product’s success. The best approach is to utilize the knowledge and experience of the P&R department.



A simple example of the types of things that can go wrong if P&R is not fully integrated into the dealmaking process is the story of inhalable insulin.

In 2001, Eli Lilly partnered with Alkermes to develop and manufacture inhalable insulin. Long believed to be an ideal replacement to injectable insulin, early clinical trials revealed that despite these initial assumptions, diabetic patients may be unwilling to switch from injectable insulin, often citing the inconvenience of carrying the large inhalation device. Moreover, among patients who may be willing to switch, payers viewed such therapies as offering convenience, not therapeutic benefit. As payers grapple with burgeoning costs, products offering mere convenience without a clear therapeutic benefit are much less likely to be covered. Ultimately, these issues led to the eventual dissolution of the partnering agreement, which could have been avoided through appropriate market analysis and a willingness to kill the project earlier, before incurring significant costs.

To help avoid failed investments, pharmaceutical companies often seek insight from pricing and reimbursement professionals who possess in-depth knowledge of the trends, issues, and reimbursement landscape. By leveraging this external analysis along with the core skill set of a pricing and reimbursement department during the evaluation of a potential licensing deal, BD teams will be able to more effectively develop the commercial value and probability of success.

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