

Axiom

Bi-annual newsletter from Pope Woodhead

Edition 1

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Our feature article

Opinion on **RISK** Management

A series of high-profile drug failures, the threat of litigation against marketed drugs and media scrutiny mean that pharma companies have to tread a very fine line between producing effective, profitable drugs, and falling foul of a risk-averse environment. But managing risk isn't unique to the pharma industry, and there are benefits for companies that take a positive approach.

Also in this issue

- discussion of the five phases to develop a successful mature product portfolio
- perspective on the markets in Poland and Spain
- update on our service offerings



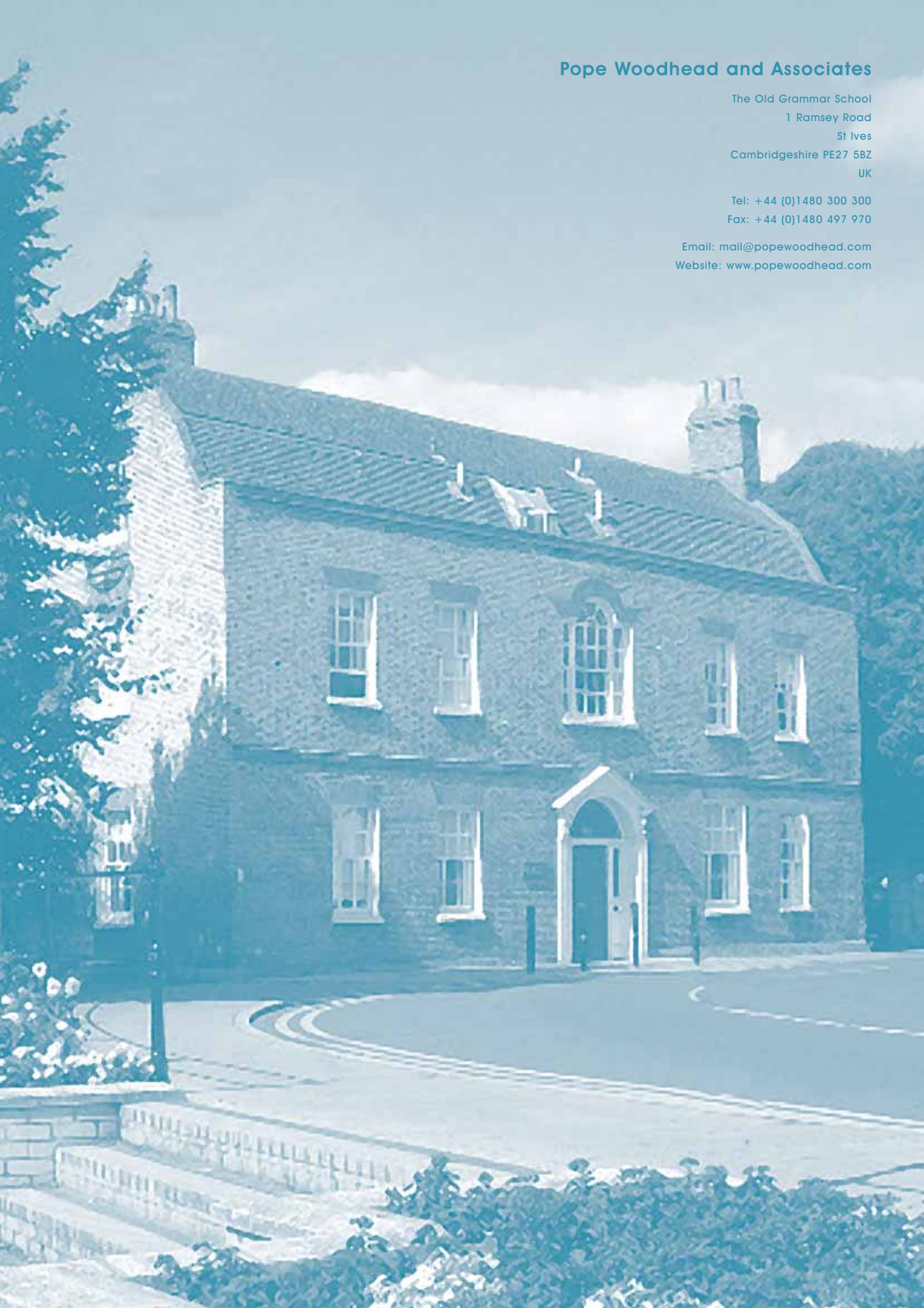
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Message from Andrew Hobbs, Managing Director

Welcome to the inaugural edition of *Axiom*. The word *Axiom* means a self-evident truth – a position from which other knowledge can be built.

With the healthcare environment undergoing significant change, areas such as market access, risk management, life cycle management and responsible care have become strategically important for many companies. At PW, we have evolved our services to help our clients address these emerging issues. Our approach continues to combine expertise with in-depth analysis and challenge to get to 'truths'. Based on this understanding we harness cross-functional knowledge to create tailored, pragmatic solutions.

In this issue we spotlight risk management – an issue that is already having a profound effect across the pharmaceutical sector and will most likely continue to do so over the coming years. With *Axiom*, our aim is to provide an informative and useful introduction to some of the issues facing the industry, and illustrate our thinking and experience on these topics as well as keeping you updated on our organisation. I hope that you enjoy reading this issue of *Axiom* during a small break in your hectic schedule. For this or any future editions I welcome any feedback you have.

Andrew Hobbs

Managing Director

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Postscript from the Chairman

Much has changed in the 25 years since I founded PW. The pharma market has matured, becoming significantly more diverse and complex. This trend will continue, yet the philosophy behind PW has remained remarkably clear: we embrace the emerging areas in healthcare and provide high-quality thinking and implementable solutions. We are continually evolving and I hope that this first edition of *Axiom* gives you a flavour of the PW of 2007.

Stuart Woodhead

Chairman

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5 phases to a profitable mature product portfolio

Author: Chris Easley

The composition of the mature product portfolio is frequently an unknown quantity for senior management in mid-size and large pharma companies. Yet 50–80% of revenues in most major pharma companies (and a higher percentage of the profit) comes from these products and active management of these assets is therefore essential.

Searching for value

Active performance monitoring and product management have traditionally been focused on new products, whilst the resources and overheads committed to mature products and the margin being achieved is rarely completely visible. This situation can be exacerbated following company mergers and acquisitions. But as new product launches dry up and revenue growth slows, companies are increasingly focusing on improved management of the mature portfolio in the search for incremental value. Three additional imperatives are driving this trend.

- Firstly, cost-sensitivity of payers is making the long-term profitability of mature products increasingly fragile. Price cuts, formulary reviews and product de-reimbursement all threaten the viability of older product classes with weaker or outdated comparator trials and health economics/outcomes research evidence.
- Payers' demands for cost-effectiveness and incentives for generic prescribing are coupled with aggressive expansion from eastern European and Asian generic players, who are making acquisitions and competing higher up the value chain. The roll-out of generics (increasingly, value-added versions) after patent expiry is also becoming more rapid across all geographies.

At a glance

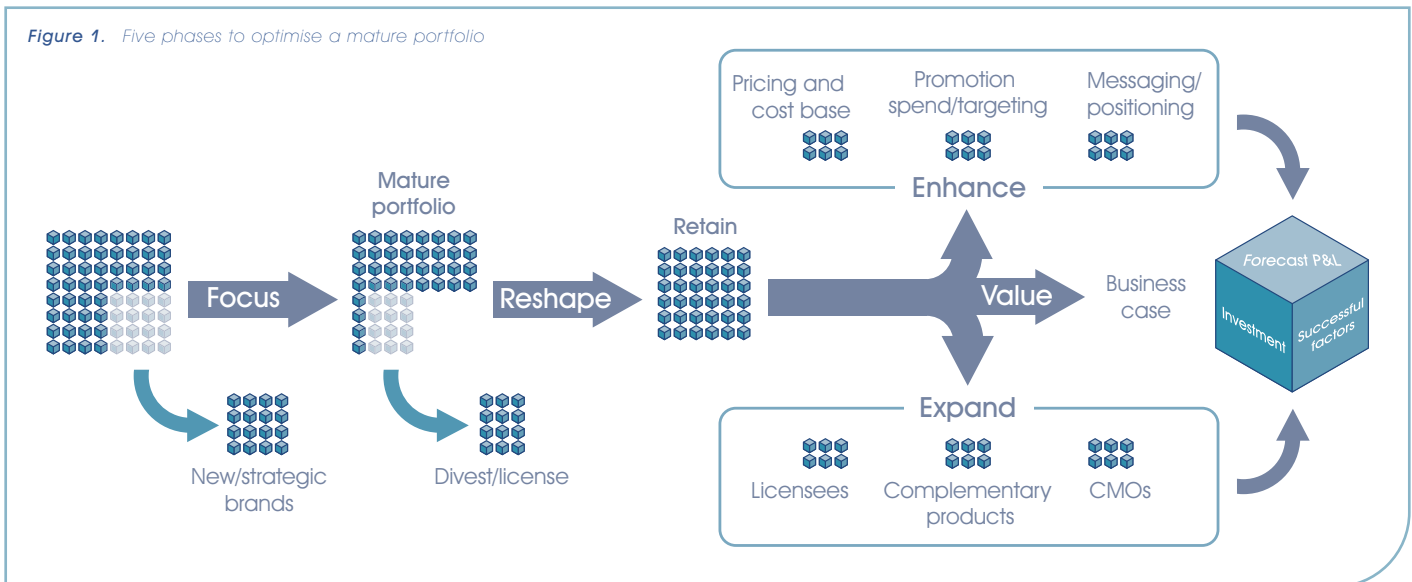
- Mature products represent 50–80% of most companies' revenues, but are rarely actively managed
- Improved management of mature products is required to meet challenges presented by cost-sensitive payers, aggressive generic competitors and fewer new products
- Leading pharma companies have been able to optimise their mature product portfolios. These activities can be grouped into five phases: focus, reshape, enhance, expand and value
- Finally, the well-documented decline in R&D productivity and shorter double-digit product growth phases are forcing pharma companies to explore other avenues for sustained growth.

Optimising profitability

The good news is that leading pharma companies have successfully implemented frameworks for optimising management of the mature portfolio; these typically comprise five phases of activity (see Figure 1).

- Phase 1: Focus – define and segment the mature portfolio based on appropriate performance metrics. Identify and collate relevant data from all markets about the company's products.
- Phase 2: Reshape – identify products no longer fitting the company's goals or those that are financially unviable. Strip these out of the mature portfolio into a separate category and assess divesture or out-licensing options.

Figure 1. Five phases to optimise a mature portfolio



- Phase 3: Enhance – identify mature brands that appear to have successfully sustained sales over time. Review current pricing, positioning and cost base; conduct a top-line assessment of potential options to create additional value through life cycle management.
- Phase 4: Expand – look at opportunities to grow the market for mature brands, e.g. use Contract Marketing Organisations (CMOs) or licensing agreements to gain better penetration or access in new markets. Assess the viability of in-licensing to complement existing mature product franchises.
- Phase 5: Value – evaluate top-line profit and loss of potential options to support the business case for selected strategies.

"...mature products can be a sizeable part of sales and profits but are not always actively managed"

Successful implementation of this process results in more than a one-time win for companies. Improvements in the management processes can be embedded in the organisation (and to some degree automated) to deliver optimal 'rolling' performance of any future products entering maturity.

Mature Products Forum 2007

the **Forum**
Mature Products
meets
Business Development
& Licensing
2007

The second PW Mature Products Forum was held at the RAC Club, London in 2007. The event brought together a select group of people working in the areas of mature products, business development and licensing.

The value of mature products in terms of steady revenue generation and often high profit margins is well recognised. However, the group acknowledged that more value could be extracted from many of these products. Barriers to this include the priority of active management and processes to enable efficient product development, cost optimisation and divestment. There was consensus that internal hurdles appeared to be the biggest barrier to extracting more value from mature product portfolios.

The key conclusions were:

- senior management within pharma needs to give greater recognition to the value of mature products and the importance of managing their growth or divestment
- regulatory functions need to be prepared for meeting the needs of mature products in addition to supporting clinical development
- dedicated leadership and resourcing is the key to driving changes in mature portfolio management.

...and 2008

Following the outstanding success of this year's Mature Products Forum, we will be hosting another event in 2008. If you are interested in taking part, please contact Stuart Woodhead on +44 (0)1480 300 300.

Opinion on **RISK** Management

Updated EU legislation means that pharmaceutical companies must generate risk management plans (RMPs) as part of the submission process. The pharmaceutical industry has to respond to this increased emphasis on risk management from regulators, and taking the right approach is now more important than ever, both pre-filing and post-launch. In this interview, Swapu Banerjee (head of the Regulatory and Risk Management practice at PW) describes how risk management can be tackled proactively, benefiting both companies and patients.

Axiom: What are the implications of the updated EU pharmaceutical code, which includes modifications to RMPs?

SB: This legislation allows the EMEA to specify conditions on an RMP as part of a marketing authorisation¹. It puts the EU slightly ahead of the USA, because the FDA requirements are only guidelines. We are now in a risk-averse climate, but I'm hopeful that risk will be seen by industry as a strategic opportunity, not just a regulatory requirement. Proactive risk management could be a differentiator between companies and competing brands.

Axiom: Risk management is now a big issue in the pharmaceutical industry. Are there comparisons with other industries?

SB: Yes, and we can learn from sectors outside pharma such as the oil and petroleum industry. Here, effective risk management is crucial to meet regulatory requirements, and it can affect the share price.

A public report into the explosion at BP, Texas City, USA was very critical of the company's safety culture and accused senior management of not taking risk and safety seriously enough*. And that's something that all corporate leaders need to be conscious of. So, the pharmaceutical industry's risk-benefit profile and the associated public perception of the safety of medicines is crucial, but not unique.

At a glance

- New EU legislation means that submissions for marketing must include risk management plans (RMPs)
- Risk management can be a strategic opportunity
- There are lessons to learn from other industries, such as the oil and petroleum sector
- RMPs are relevant from phase II through to post-launch
- They require good cross-functional teamwork
- PW uses FMEA (failure modes and effects analysis) to pinpoint risks in the treatment pathway
- Well-developed tools are the cornerstone of a successful risk management plan

"...the pharmaceutical industry's risk-benefit profile and the associated public perception of the safety of medicines is crucial, but not unique."

1. The European Parliament and the Council of the European Union. Directive 2004/27/EC of the European Parliament and of the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use. April 30, 2004.

* The BP Texas City (USA) refinery explosion in 2005 killed 15 workers and injured 180. A subsequent investigation and US Chemical Safety Board Report alleged that BP directors "did not exercise effective safety oversight".

Axiom: Which attributes should every risk management programme have?

SB: Good multi-disciplinary team working and communication is very important. Commercial aspects of drug development may not always be seen by the safety department, but equally the commercial side of the business isn't always aware of the safety constraints and regulations (see 'Survey reveals risk awareness gap', on the back page). A consultancy such as PW can assess the overall picture using experience gained from working across different functions. We can advise on and facilitate cross-functional risk management processes, both to the client's benefit and, ultimately, for the safety of patients. This means that good risk management can become a distinct competitive advantage.

Describing an effective way of evaluating risk management tools is also an important part of any RMP. We use FMEA (failure modes and effects analysis) to pinpoint where risk tools are needed in the treatment pathway. This provides logical reasoning for selecting specific tools in the RMP. We are also developing innovative ways of evaluating the success of RMPs that have already been rolled out.

Axiom: The industry is entering a new era of risk management, but how prepared are pharma companies to deal with this, and what is your advice to those who work in this area?

SB: Risk in mid-size companies tends to be dealt with by the safety department. Risk management processes have only been running for a couple of years, which often restricts experience to a single-company view, leading to a safety rather than strategic focus. It is useful to meet with specialists from different areas and learn how other companies manage risk. Internally, ask for input from different groups and make sure that stakeholders are aligned. Safety is paramount, but receiving input from clinical development and the medical, regulatory and marketing functions, together with senior management's perspective, is necessary too. External communication to patients, where necessary, and prescribers is also very important. The tools selected for this task must be of excellent quality because they are the cornerstone of a successful RMP.

Axiom: How do you think risk management might develop in the current risk-averse environment?

SB: A more proactive approach should be considered, which is also a requirement of EU legislation and FDA guidance.

"Companies are approaching us at phase II and then planning their phase III plans from a risk-benefit angle, not just from a safety, efficacy and quality standpoint."

An RMP is necessary for new biologics and molecules with a novel mode of action where they might impact on public health. It should not just be developed in a hurry at the time of filing. At PW we can generate and offer advice about developmental RMPs. Companies are approaching us at phase II to add a risk-benefit angle to the safety, efficacy and quality parameters in their phase III plans.

Class effects of drugs become more prominent post-launch, and a company may divest, in-license or out-license a drug based on risk issues that affect its whole class. So, assessing the risk-benefit profile is crucial throughout the whole product life cycle. Risk communications can also become more innovative, which is an area of great potential growth.

Further information

FMEA approach to risk

- Proactive technique with the aim of preventing adverse events before they occur
- Analyses risks of component parts in a system, in terms of likelihood and impact
- Risks that would concern regulatory authorities are identified
- Measures to mitigate these risks are designed and implemented

Focus on Poland

Author: Malgorzata Zienowicz

The Polish market is forecast to be worth US\$5.9 bn in 2010, but innovative drugs look set to take only a fraction of the market share.

Poland's Ministry of Health (Ministerstwo Zdrowia) has traditionally favoured reimbursing generic drugs produced by domestic manufacturers, and budgetary restrictions have led to very few innovative drugs receiving funding. For example, leading global products such as GSK's Seretide® and Sanofi-Aventis' Plavix® do not feature on Polish reimbursement lists. Generic medicines currently dominate the Polish market, representing over 60% of the market in value and 85% in quantity. An overall trend towards lower prices during 2006 does not suggest a change ahead, so how might an innovative drug make an impact in such a price-sensitive market?

Anticancer drug prices up

Providing improved care in some areas means introducing innovative drugs. For example, the National Programme for Combating Cancer was launched in 2006, a year that saw anticancer prices rising by 26% between January and October. This was driven by the inclusion of anticancer medicines onto the list of therapeutic products used for in-patient care, which are used by hospital committees to select treatments for individual diseases.

In addition, the Polish Ministry of Health has made a promise to add 52 innovative drugs to the reimbursement lists during 2007. Whether this promise will be completely fulfilled is unclear. Dismayingly, in October 2006 the Ministry of Health negotiated a price reduction of 270 drugs used in public hospitals. Drug prices in hospitals are now 10% lower than market rates and 6% lower than prices previously agreed with pharmaceutical companies.

Unfortunately the criteria for reimbursement are not always completely transparent, and the overall trend in hospitals is still towards lower prices. Without inclusion on the reimbursement lists in Poland, funding for an innovative drug can only be achieved in two ways: through a 'special drug programme', approved by the national health service (Narodowy Fundusz Zdrowia), or as a 'targeted import' approved by the Ministry of Health.

At a glance

- Generic drugs dominate the Polish market
- Very few innovative drugs receive reimbursement
- Drug prices in 2006 were reduced, although the market grew by more than 4%
- Reimbursement procedures should be streamlined during 2008
- Achieving reimbursement and better prices is more likely if linked to a specific government health programme

Outlook

The next 12 months should bring reforms and greater transparency to reimbursement procedures as Poland gradually moves into line with other EU countries. These reforms will include:

- introduction of an appeals procedure
- a scientific commission/committee for evaluating applications, based on scientific, pharmacoeconomic and budgetary data
- publication of review criteria and the rationale for decisions.

Additionally, efforts are being made to stimulate innovation amongst Poland's underdeveloped biotechnology sector. The Polish Academy has outlined a plan that recommends more investment in science parks, better co-operation between industry and academia, attracting more EU funding and developing local goals for high-tech industry in targeted regions of Poland. This may eventually lead to a more receptive environment for innovative drugs in Poland, but opportunities for reimbursement in the short term are likely to be limited to government-approved health programmes.

Focus on Spain

– market access

In a recent article in *Pharmaceutical Marketing Europe*, Dr François Lucas (head of the Marketing Insights and Strategy practice at PW) provided his perspective on the pricing and reimbursement challenges for new drugs in his country of residence, Spain. François highlighted the importance of having a value proposition based on what payers need and can accept supported by relevant evidence.

Historically, Spain has been fairly unrestrictive in providing reimbursement for new drugs, but in common with other EU countries, a transition to tighter control of drug prices and greater use of generics is underway. The July 2006 medicines bill included cost containment measures affecting 'me-too' and already marketed drugs, so real innovation and benefits based on clinical and health economics evidence must be demonstrated if reimbursement is to be achieved.

Good communication with payers and their influencers is also a critical component of a successful reimbursement strategy. Affiliate organisations have knowledge of, and relationships with, the multiple stakeholder groups. This is certainly true in Spain, where groups exist on three levels:

- national (Health Ministry and the Health Technology Assessments [HTA] body)
- regional (17 autonomous communities, each with their own health authority, HTA body and pharmacists)
- local (hospital formulary committees).

The value proposition and relevant evidence may need to be presented to each of these stakeholders. Doing this in a way that addresses their particular needs and perspectives but retains consistency may demand new skills in the local organisation. One way that global functions can support local activity is through the provision of a market access toolkit that provides:

- the core value proposition and key messages
- relevant evidence and supporting materials in a form that supports local adaptation
- locally relevant data.



PW practices

It's possible that you've met one or two of the PW management team already, but not really had the chance to get to know what each of the practices really has to offer. A snapshot of PW's service offerings is illustrated below.



Beverly Barr
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Communications

Intelligent communication solutions – translating evidence into value

In a complex and demanding market environment, evidence-based, targeted communications are essential for success. Using a consultancy-led approach, we provide communications strategy and tactics to address key industry challenges.

Our services

- Market access and pricing & reimbursement materials/publications
- External affairs
- Value dossiers and slide kits
- Market access training
- KOL management
- Risk communications; patient, physician and pharmacist education/outreach materials
- Risk management training (global and affiliate)
- Disease area awareness and compliance programmes



Michelle Short
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Process Design and Implementation

A structured approach – unlocking the real potential of people and projects

Our key areas of expertise are interdisciplinary product strategy development, global-to-local planning and knowledge sharing.

We help our clients to achieve optimal working practice through the creation or improvement of internal processes and their effective implementation through better cross-functional teamwork and two-way global-to-local dialogue.

Our services

- Stakeholder consultation
- Process mapping and validation
- Facilitating cross-functional alignment
- Organisational development including KPIs and HR requirements
- Development of tools to aid implementation
- Communication and training to embed new or refined processes
- Integration with other processes



Lia McLean
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Regulatory and Risk Management

Successful risk management systems – in a new era of global drug safety

Increased emphasis on risk management from the regulatory authorities means that risk management planning is now a critical component of bringing a new product to market – and of maximising its potential by keeping it there.

As thought leaders in the regulatory, risk management and drug safety arena, we help our clients address strategic risk management problems from early development to post-marketing. In particular we provide a vital link to integrate this thinking with the commercial strategy.



Swapu Banerjee
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Our services

- Risk management planning (RMP, RiskMAP, DRMP)
- Regulatory submission support, including health authority communications
- Risk management programme design and implementation
- Governance and infrastructure requirements
- In- and out-licensing opportunity and risk assessment
- Regulatory risk assessment and management
- Regulatory challenge panels
- Label reviews
- Quality and compliance programmes.

Market Insights and Strategy

Turning insights into action – commercial clarity in a complex market

Understanding the dynamics and value drivers in today's complex markets is critical to success. With the value of every new medicine under the spotlight, a clear value proposition as well as a robust strategy for market entry, market access and reimbursement are key.



François Lucas
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Our services

- Market mapping to define the market context and dynamics
 - Stakeholder insights including payer research
 - Value proposition development
 - Identification of the value levers and evidence requirements
 - Market entry, market access and life cycle management strategy development and validation
- In an increasingly crowded and competitive market, optimising the value of assets can be critical.**
- Our approach to portfolio management has been used to:**
- optimise the value and minimise risks of mature product portfolios
 - develop and implement therapeutic area portfolio strategies.

Bulletin Board

New faces at PW

Lisa Alderson, Malgorzata Zienowicz, Chris Easley and Andrew Heggie have joined PW this year.

- Lisa started in the business development team in April and believes that "there is a lot of change happening in the industry, making it an exciting time to be working at PW".
- Malgorzata joins the Regulatory and Risk Management practice. Her experience includes lecturing on clinical pharmacology at Warsaw University and working for the Polish Regulatory Agency as an external expert.
- Chris has been appointed senior consultant in the Market Insights and Strategy practice. His extensive experience in product life cycle management will assist clients in two increasingly important areas – market access and optimising the profitability of companies' mature product portfolios.
- Andrew joined the Process Design and Implementation team in September. His previous experience has been with the Elanco division of Eli Lilly & Co and King's College London Business Ltd where he took technologies through the in- and out-licensing partnering processes.

Keynote speech on strategic risk assessment

Early-stage developmental risk management is more important than ever. This was the message delivered to the audience by PW's Dr Swapu Banerjee, in a keynote speech at the Biofine global conference held at Barcelona in the spring.

Swapu emphasised that safeguarding patients and healthy volunteers is of paramount importance, but risk assessments are also of strategic commercial importance for large pharmaceutical companies and smaller biotechs who are assessing licensing opportunities. He added that there is evidence to show that a developmental risk management plan (DRMP) can increase the value of small molecules as well as biotechnology products, including biosimilars. A novel model for early-stage risk-benefit assessment of biosimilars is currently being developed by the PW Regulatory and Risk Management practice.

Future life science industry leaders at PW

As part of PW's ongoing collaboration with the Institute of Biotechnology at the University of Cambridge business school, three future bioentrepreneurs chose to work with PW on their research projects. Beatriz Senan-Castellano, Olivia Lefebvre and Lars Gredsted all wrote research-based dissertations that will contribute to their Masters in Bioscience Enterprise. Swapu Banerjee, one of PW's intern supervisors, commented, "the research projects look at current strategic opportunities and challenges within global pharma and biotech. Partnering with the University of Cambridge keeps PW at the forefront of thought leadership in product development and marketing strategy. It also fosters the knowledge-driven ethos at PW that supports our services." Findings from each intern's dissertation will appear in the next issue of *Axiom*.

Survey reveals risk management evaluation skills missing

PW recently published the results of a risk management awareness survey in *Drug Safety*. Unsurprisingly, those who work in drug safety had a greater awareness and understanding of EMEA/FDA risk management guidance than those in other functions. The survey also highlighted the need to embed risk management knowledge throughout the organisation and to integrate a 'safety first' mindset into the commercial strategy. Most organisations in the survey felt they did not have the requisite skills or processes to evaluate their risk management programmes and tools, despite this being a requirement of the EU-RMP legislation.