

# Setting the stage for risk-sharing agreements: International experiences and outcomes-based reimbursement

Carapinha JL, BPharm(Wits), MM, P&DM(Wits)

PharmaLogica

Correspondence to: João L Carapinha, e-mail: info@pharmalogica.net

## Abstract

**Background:** Biological medicines are clinically effective but very expensive in South Africa. The business decisions of biological manufacturers and payers (medical schemes) impact the access patients have to biological medicines. This paper presents risk-sharing agreements as a means of managing the risk of introducing biological medicines into the healthcare market.

**Methods:** The paper critically reviews literature of some prominent international experiences with risk-sharing agreements and the nuances associated with such agreements. The paper also critiques the outcomes-based reimbursement of biological medicine and the structural necessities for its successful implementation.

**Results:** A risk-sharing agreement is a useful tool to manage the risk of introducing clinically effective and very expensive medicines into the healthcare market. It is also a tool that bridges the conflicting priorities of the manufacturer of biological medicine and the payer.

**Conclusion:** The application of risk-sharing agreements within an international context informs the local discussion. This paper is the first in a two-part series that serves to review the international experience with risk-sharing agreements and critique the outcomes-based reimbursement of biological medicines. The backdrop is set for a discussion of the application of risk-sharing agreements in South Africa, which is the purpose of the second paper in this series.

Ⓟ This article has been peer reviewed. Full text available at [www.safpj.co.za](http://www.safpj.co.za)

SA Fam Pract 2008;50(4):62-65

## Introduction

Biological medicines are clinically effective but very expensive in South Africa. These medicines are produced using a living organism, are complex protein structures typically much larger than traditional chemical medicines, and are mostly administered by injection. Biological medicines are more advanced than conventional therapies and provide prescribers with enhanced tools for treating patients. Access to biological medicines is a contested terrain between the manufacturer of biological medicine and the payer (medical scheme), often to the detriment of the patient. A risk-sharing agreement is a tool for manufacturers of biological medicines and payers to manage the risk of introducing clinically effective and very expensive medicines into the healthcare market. As promising as the approach may seem, particularly for patients, risk-sharing agreements come with some challenges to their implementation.

In this first paper in a two-part series, risk-sharing agreements are discussed from an international perspective. The second paper discusses risk-sharing agreements with reference to events in 2006 involving trastuzumab (Herceptin®) and Discovery Health. This case carries within it many of the critical elements of risk sharing

that merit further discussion. The second paper also explores the policy implications for the manufacturer and payer of entering into risk-sharing agreements. It then concludes with policy guidelines for risk-sharing agreements in South Africa. However, in order to discuss risk-sharing agreements in South Africa, first a discussion of the international perspective is required. That is the purpose of this paper – to contextualise a local discussion against the backdrop of some prominent international experiences with risk-sharing agreements, outcomes-based reimbursement and the structural necessities for these agreements.

## International experiences

Risk-sharing agreements have been used in both Australia and the United Kingdom. However, the conceptualisation and application of these have taken on slightly different approaches. The nuances of each risk-sharing agreement allow for some flexibility around the amount and type of risk assumed by each party.<sup>1</sup>

Risk-sharing agreements in Australia refer to the ability of the government to recoup from the manufacturer of high-cost medicine a percentage that exceeds the annual budgeted amount for the

managed consumption of a new medicine.<sup>2</sup> For instance, if the annual government budget for a new medicine is A\$250 million and the actual expenditure is A\$270 million, a percentage of the difference of A\$20 million would be recouped from the manufacturer. It may also include a price decrease if the annual expenditure exceeds predetermined thresholds.<sup>2</sup> Such arrangements are referred to as price-volume arrangements, according to which, if a specific volume of sales is attained, the manufacturer is obliged to lower its price of the medicine. Risk-sharing agreements provide some certainty for the government regarding pharmaceutical expenditure. The risk-sharing agreements are structured in such a way that the manufacturer is disincentivised to exceed the annual budgeted amount.<sup>3</sup> In Australia, there are currently 14 such agreements in place (the first was made in October 2003) with more being negotiated with manufacturers.<sup>2</sup> Risk-sharing agreements are monitored monthly with Medicare data for each medicine.

Even if the annual threshold is exceeded it does not prevent the use of the medicine. Risk-sharing agreements are accompanied by predicted versus actual systematic analysis (PvA). A PvA is a review that compares the expected consumption and expenditure to actual consumption and expenditure. It is also often referred to as a budget-impact analysis. It is from this review that the annual budget amount is calculated. However, in few cases have these annual amounts been reached, calling into question the accuracy of the budgeted amount. Risk-sharing agreements were only expected to reach 64% of the budgeted amount.<sup>2</sup> PvAs were found to be ineffective at comparing expected versus actual data. This, however, does not negate the importance of PvAs but indicates that further resources are required to ensure their effectiveness.

Other risk-sharing agreements have directly linked the price of a medicine to actual patient survival rates.<sup>4</sup> The price of the medicine will decrease if the observed mortality rate is not within expected parameters. That is, the price would decrease to ensure that the same cost-effectiveness parameters are maintained. Similar approaches have been mathematically modelled to provide a tool with which to maintain this balance.<sup>5</sup>

In the United Kingdom, the North Staffordshire Health Authority, Pfizer and Keel University partnered to establish a risk-sharing agreement for the treatment of high cholesterol concentrations with atorvastatin.<sup>6</sup> The agreed outcome measure was the achievement of a low-density lipoprotein cholesterol concentration target of less than 3 mmol/l. A matrix was developed and modelled on clinical trial data. It detailed the percentage of patients expected to attain the outcome measure at specific doses of atorvastatin within specified cholesterol severity categories. Failure to adhere to the agreed outcome measures triggered a refund of the cost of the medicine by the manufacturer. The refund was based on the cost differential between the expected and observed outcome measures.

Multiple sclerosis (MS) and the use of interferon beta and glatiramer acetate in the United Kingdom also formed a platform for debate on risk-sharing agreements – a debate that has striking similarities to the case of trastuzumab and Discovery Health. These include the following issues: what constitutes cost-effective therapy, the application of thresholds to determine funding, and the role of an independent agency to guide decision making.<sup>7</sup> The National Health Service (NHS, Department of Health) announced, contrary to the recommendation of the National Institute of Health and Clinical Excellence (NICE) that 10 000 MS patients would be treated with interferon beta and glatiramer acetate.<sup>8</sup> Eligible MS patients would be treated and monitored and the NHS would fund the medicine until it was deemed no longer effective.

The price of the medicine would decrease if the observed outcome measures did not correspond with the expected outcome.

There are numerous weaknesses in this risk-sharing agreement for MS patients. Each of the weaknesses point to the scientific and practical robustness of the facts used to guide the final risk-sharing agreement.<sup>9</sup> The scientific weaknesses include: the non-randomised comparison of modern and historical cohorts which may provide unreliable and biased results; the lack of power calculations, which may result in inaccurate measurement of the treatment effect; other biases that include inappropriate inclusion criteria, monitoring of patients that drop out, and the lack of blinded assessment of the treatment outcome; and the array of assumptions used in the model to calculate the cost-effectiveness of the treatment. Practical weaknesses include: the timely establishment of a risk-sharing agreements co-ordinating committee; additional resources required to cope with the data-intensive (collection and analysis) process; and the communication of protocols (rules and conditions) to participating prescribers before implementation.

Payers have identified that gaps exist between medical claims in clinical trials and the medicine's use after launch. Payers are therefore allocating resources with which to monitor medicines during their post-marketing phase.<sup>10</sup> Payers have recognised that data collected to describe an average patient in a highly restricted clinical trial should be used cautiously to predict treatment effects in a greatly expanded patient population. Payers are aiming to manage the risk associated with these gaps by introducing risk-sharing agreements. Sensitivity analyses around the key variables during the economic modelling process enable payers to better understand the relative contribution of each key variable. Acceptable therapeutic and financial parameters are derived during this process and incorporated into risk-sharing agreements.

### Outcomes-based reimbursement

Many risk-sharing agreements have only been concerned with the objective of decreasing the price of biological medicine. Unfortunately, little attention has been given to the ability of biological medicine to achieve defined clinical outcomes and desirable quality of life (QoL) outcomes for patients. Some risk-sharing agreements have considered the financial risk alongside the clinical and QoL risk. However, there have been no attempts to measure these outcomes in a systematic and standardised way among patients to enable meaningful comparisons. The outcomes-based reimbursement of biological medicine is a method of addressing the inherent weakness of only considering risk-sharing agreements as a financial risk management tool.

The outcomes-based reimbursement of biological medicine involves a process of reimbursing the manufacturer of biological medicine for achieving defined clinical outcomes and improving the QoL of the patient within agreed financial parameters. Such an approach requires ongoing monitoring by all parties to the agreement to ensure that results of the biological medicine evidenced in clinical trials is comparable to clinical practice. This may include the ongoing collection of clinical practice data by the healthcare provider. The payer may also choose to administer regular QoL measurement tools with which to assess the progress of a patient. Unfortunately, most payers' data-management systems are superlative cost-management tools with a crippling inability to monitor a patient's clinical progress. This problem is also evidenced in the context of Health Maintenance Organisations (HMOs) in the United States of America (USA).<sup>11</sup>

Outcomes data could be integrated into a single source of information with which to better manage a risk-sharing agreement. Some risk-sharing agreements have used a patient registry to centrally manage all parameters.<sup>4</sup> The collaboration of numerous stakeholders assists in addressing issues of efficiency and cost-effectiveness that ultimately shape the final form of the risk-sharing agreement.<sup>3</sup> In the United Kingdom, risk-sharing promoted the reimbursement of medicine that met agreed outcomes. Failure to adhere to the agreed outcomes meant that the manufacturer had to refund the government for the cost of the medicine. The outcomes-based reimbursement of biological medicine assumes that there is: a) widespread use of best available evidence in all clinical settings; b) adherence of prescribers to treatment algorithms; c) continuous provision of high-standards of pharmaceutical services by dispensers; and d) an educated and assertive patient population.

The outcomes-based reimbursement of manufacturers also requires that payers factor into their reimbursement policies the indirect benefits associated with biological medicines. The societal perspective of economically evaluating the value of a medicine is often not considered by payers. Biological medicines can contribute to an improvement in the productivity of the patient and thus an ability to earn an income and ultimately contribute positively to the social and economic development of a country. Every additional patient that is kept in the labour market results in the potential to develop the country further. However, little research has been done in developing countries to quantify the overall economic contribution of each person active in the labour market. Moreover, there is little research conclusively quantifying the contribution of biological medicine to the economic development of a developing country.

In addition, the ability of a patient to earn an income also ensures that the patient has the ability to pay the monthly contribution and remain insured with a private payer. It also prevents the patient from adding to the growing burden of healthcare services offered by the public sector. The household is also dependent on the income generated by the insured patient. Without this source of sustaining the livelihood of the household, the dependents of the income-earner will inevitably also become dependent on the public sector for their healthcare services. Little research has been done to quantify the impact of the above dynamic in developing countries.

A challenge exists to determine the effect that external factors, namely patient compliance and the inefficient delivery of healthcare services, have on risk-sharing agreements. The latter is a perennial challenge in developing countries – for instance the availability of skilled healthcare workers to monitor all patients receiving a biological medicine, and the necessary infrastructure and processes to support the monitoring requirements. Inefficient healthcare services will hamper the ability of biological medicine to achieve its full therapeutic benefit.<sup>10</sup> The challenge in developing countries is to identify these inefficiencies and to develop tools to accurately predict their impact on risk-sharing agreements.

### Structural necessities

There are two structures required to enable the outcomes-based reimbursement of biological medicine. The first is the initiation of a structure similar to the National Committee for Quality Assurance (NCQA) in the USA.<sup>12</sup> Such a structure would assist patients with comparing health insurance products offered by payers. A comparison

of the different products could be based on their ability to provide quality healthcare services, overall cost to the patient and ability to improve QoL. This information will enable patients to make more informed healthcare purchasing decisions. Patients would, for example, be provided with information on the internal quality-control procedures of the payer, range of healthcare provider contracts, and utilisation management procedures.<sup>12</sup> The information generated by such a structure would assist the payer and the manufacturer to tailor a risk-sharing agreement to the risk profile of the patient population insured by the payer.

The above domain is already regulated by the Council for Medical Schemes; however, there are projects that could immediately be self-initiated and self-regulated by payers.<sup>13</sup> One such project may include implementing an outcomes-measurement database that enables the comparison of one payer with another. Payers may choose to develop numerous standardised indicators with which to compare each other. These may include effectiveness of care, reduction in disease-specific incidence rates, access to healthcare services, patient satisfaction with healthcare service-provider networks, and improvement in QoL, to name a few. This information must be made available to the public to encourage better healthcare decision making.

The second structure required for the outcomes-based reimbursement of biological medicine is a structure comparable to the National Institute of Health and Clinical Excellence (NICE) in the United Kingdom. Such a structure would aim to review all the best available clinical evidence and provide recommendations to the private and public health sectors for the reimbursement of medicine. The structure would be a useful repository of evidence-based medicine resources and provide useful tools to strengthen clinical governance in health settings.<sup>14</sup> In addition, the structure would enable a robust mechanism for benchmarking current clinical practice to the recommended approach. Such a structure would aim to develop standardised methods of measuring clinical outcomes associated with the use of biological medicines in clinical practice. The information generated by this structure would address the information asymmetry between the payer and the manufacturer.

### Conclusion

It is not clear whether the conditions in a risk-sharing agreement adversely impact on an individual patient's clinical and QoL outcomes. Risk-sharing agreements have also not been assessed to measure their effectiveness in containing pharmaceutical expenditure. A weakness of the process is incomplete and inaccurate data at the commencement of risk-sharing agreements, which may materially impact on the measurement of observed outcomes (cost, clinical and QoL). In addition, an assessment is required of whether risk-sharing agreements have inadvertently resulted in the underutilisation of biological medicines. Further research is needed.

A risk-sharing agreement is a useful tool to manage the risk of introducing clinically effective and very expensive medicines into the healthcare market. It is also a tool that bridges the conflicting priorities of the manufacturer of biological medicine and the payer. This paper has discussed international experience with risk-sharing agreements. There are numerous approaches to the use of risk-sharing agreements. The international experience with regard to risk-sharing agreements is not uniform and differences exist in each agreement, as emphasis is placed on particular elements and not on others. A single

and universally accepted model for risk-sharing agreements is unlikely and will most probably be ineffective in vastly different healthcare structures in developing countries. Each risk-sharing agreement must be customised for the specific market's need but still adhere to the objectives of a risk-sharing agreement.

The paper also discussed the outcomes-based reimbursement of the manufacturer of biological medicine as a mechanism of rewarding the achievement of defined clinical outcomes and improving the QoL of the patient within agreed financial parameters. This approach would require structures similar to the NCQA and NICE to facilitate better healthcare decision making and address market failures such as information asymmetry in the healthcare market. Against this backdrop it is now possible to proceed with a discussion of the application of risk-sharing agreements for biological medicines in South Africa. This is the purpose of the second paper in this two-part series.

### Declaration

The author is the owner of PharmaLogica, a consulting company active in South Africa and the United States. Its aim is to respond with effective and innovative insight to the needs of the pharmaceutical sector in developing countries. PharmaLogica has worked for non-profit institutions and government agencies and has also consulted on a project basis for pharmaceutical companies. This research was self-initiated by the author and funded by PharmaLogica. The author's views are his own.

### References

1. Cherney A. Choosing an advantageous risk-sharing arrangement. *Healthcare Financial Management* 1999 March. [Accessed 19/12/2007] Available from: [http://www.findarticles.com/p/articles/mi\\_m3257/is\\_3\\_53/ai\\_54172072](http://www.findarticles.com/p/articles/mi_m3257/is_3_53/ai_54172072)
2. Australian National Audit Office. Selected measures for managing subsidised drug use in the Pharmaceutical Benefit Scheme, report no. 44. [Accessed 20/12/2007] Available from: [http://www.anao.gov.au/uploads/documents/302804\\_Audit%20Report%2044-5.pdf](http://www.anao.gov.au/uploads/documents/302804_Audit%20Report%2044-5.pdf)
3. Lu CY, Williams K, Day R, et al. Access to high-cost drugs in Australia. *BMJ* 2004; 329: 415–6.
4. Wlodarczyk JH, Cleland LG, Keagh AM, et al. Public funding of bosentan for the treatment of pulmonary artery hypertension in Australia: cost effectiveness and risk-sharing. *Pharmacoeconomics* 2006; 24 (9): 903–15.
5. Zaric GS, O'Brien BJ. Analysis of a pharmaceutical risk-sharing agreement based on the purchaser's total budget. *Health Economics* 2005; 14: 793–803.
6. Chapman S, Reeve E, Rajaratham G, et al. Setting up an outcomes guarantee for pharmaceuticals: new approach to risk-sharing in primary care. *BMJ* 2003; 326: 707–9.
7. Taylor D. Funding medicines for people with multiple sclerosis. *BMJ* 2001; 323: 1379–80.
8. Little R. NHS to fund treatment for 10 000 patients with MS. *BMJ* 2002; 324: 316.
9. Sudlow CLM, Counsell CE. Problems with UK government's risk-sharing scheme for assessing drugs for multiple sclerosis. *BMJ* 2003; 326: 388–92.
10. De Pouvourville G. Risk-sharing agreements for innovative drugs. *Eur J Health Econ* 2006; 7: 155–7.
11. Abernathy M. Avoid common problems in risk-sharing contracts. *Managed Care* 2000; April. [Accessed 19/12/2007] Available from: <http://www.managedcaremag.com/archives/0004/0004.risk.html>
12. O'Kane ME. Accreditation and performance measurement programs for managed care organisations. In: Kongstvedt P, editor. *The Managed Health Care Handbook*. Maryland: Aspen; 2001. p. 849–70.
13. Council for Medical Schemes. Annual Report of the Registrar of Medical Schemes, 2002/2003. [Accessed 13/04/2007] Available from: <http://www.medicalschemes.com>
14. National Institute of Clinical Excellence. About NICE. [Accessed 13/04/2007] Available from: <http://www.nice.org.uk/page.aspx?o=aboutnice>