Dear readers,

Following the successful proceedings of the first Health Technology Assessment Conference, organized in Athens on November 5th, 2015 Health Daily and Boussias Communications are proud to present in this special edition the first paper as a result of the work conducted by one of the main speakers Mr. Martin Price, Vice President, Market Access EMEA, Janssen on the implications of HTA for national policy from an industry perspective. In light of our forthcoming HTA Conference on February 7, 2017, this paper is most important as it sets a precedent and food for thought for the imminent discussion on building trust and identifying national barriers as a basis for creating an integrated HTA platform in our country. We would like to thank Mr. Price for keeping his promise and following through with this important work.

HEALTH TECHNOLOGY ASSESSMENT – IMPLICATIONS FOR NATIONAL POLICY: AN INDUSTRY PERSPECTIVE

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Target audience
Policy makers in middle and low income countries considering the introduction and development of health technology assessment (HTA) at a national level

Target journal
NA - Conference proceedings following presentation at HTA conference in Greece

Key words:
Health Technology Assessment, balanced assessment, decision-making, health economics, pharmaceutical assessment

Strategic aim of manuscript
Publish an industry perspective on the key principles of HTA to support the introduction of nationally relevant, rational and affordable systems in countries considering implementing HTA.

Key messages
• HTA is a tool to assess value, it should consider the societal, ethical, organisational, economic and legal implications for the healthcare system
• HTA needs to guide rational healthcare decision making relevant to the jurisdiction
• HTA assesses value, ‘where to invest’, it does not identify ‘how much to invest’
• Affordability assessment enables managed entry
• Industry has an important role to play as a key stakeholder within HTA at policy, reimbursement and pricing levels

Abstract
Introduction and objectives: Due to limited resources, health systems are increasingly looking to health technology assessment (HTA) as a tool to guide health policy decisions. There are a range of models used in HTAs across the European countries including the “relative effectiveness” followed by Germany and France, and the “cost/quality adjusted life year (QALY)” used in the UK. Pharmaceutical companies need to navigate different systems and value assessment criteria to ensure patient access to new medicines. There are examples of good practice in a number of HTA systems; however, current systems often suffer from complexity, lack of transparency and limited focus to patients. The objective of this review was to provide an industry perspective on the key principles of a national HTA system that would balance the needs of payers, healthcare professionals, patients and industry.
**Discussion:** From an industry perspective, the key principles for a nationally relevant, rational, effective and patient-focused HTA system should include transparency, stakeholder engagement, independence of HTA assessment bodies and payers, accountability, a locally relevant scope and an appropriate evidence framework. Dialogue between decision-makers and industry is key to discuss the value assessment, pricing and patient access arrangements. As evaluating affordability is not the remit of HTAs, patient access schemes (e.g. risk sharing, confidential discounts or price capping), are valuable in addressing potential affordability issues. A system that values new therapies on the basis of clinical benefit and subsequently enters a negotiation period with payers may lead to better outcomes for patients compared with systems driven by rigid cost-effectiveness thresholds.

**Conclusions:** There is no single “right” HTA model, but good practice elements exist across different systems in Europe. Although sharing HTA experience across countries is beneficial, decisions based on HTA need to remain a national responsibility. Countries who are considering introducing HTA need to define processes that reflect national competence and address local priorities.

**Introduction**

Health systems, however diverse, share a common goal to improve the health of their population. The financing and delivery of health services is a critical aspect in being able to achieve this goal of health gain. With limited resources, health systems are increasingly looking to health technology assessment (HTA) as a means to guide health policy decisions. HTA, a multidisciplinary process that summarises the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased and robust manner, informs the formulation of safe and effective health policies that are patient focused and achieve best value for the jurisdiction. This article provides an industry perspective on the key principles that should be considered inherent to the establishment, conduct and implementation of national HTA.

**Current situation**

Looking at established HTA processes in Europe, two main models have evolved around the value framework, namely the “relative effectiveness” and the “cost/quality adjusted life year (QALY)” approaches (Figure 1). The “cost/QALY” (CPQ) model provides estimates around the incremental costs per QALY gained and aims to assess the cost-effectiveness of new interventions against an acceptable incremental cost-effectiveness ratio (ICER) threshold (e.g. £30,000 per QALY gained for the National Institute for Health and Care Excellence [NICE] in the UK). One potential benefit of this model is its explicit robust methodological criteria. Drawbacks are said to include its reliance on often complex modelling, resulting in technical complexity, statistical uncertainty, and difficulty for stakeholders to understand results and implications. In addition, there is debate about what an appropriate ICER threshold should be and how clinically relevant the QALY metric is when the focus of HTAs are patients. “Relative effectiveness” models tend to evaluate new technologies in terms of the clinical outcomes and added benefit they provide patients, compared with the current standard of care. Typically, an evaluation process is undertaken during which the added clinical value of the new technology is characterised relative to standard of care. Once this has been finalised, the outputs of the evaluation are used as inputs into price negotiations between the company and the relevant national authority. The more intuitive concept of this model makes it easier for key stakeholders to understand the basis...
for the assessment determination, and it provides greater flexibility in patient access discussions. However, one potential issue is that determinations on the level of added benefit may be considered to be less transparent than those based on very clear cost-effectiveness acceptability thresholds.

In both models, the assessment and the appraisal components tend to be separated, which is an important principle of HTA. The assessment evaluates the clinical and/or economic evidence (including strength, uncertainty and academic rigour) and is often undertaken by academic/scientific groups. The appraisal component is the decision making process, which uses the findings of the technical review and considers broader health policies, as well as cultural or social factors in the interpretation of the evidence. The reimbursement price of the medicine is typically also negotiated during this process. Examples of these models in Europe include France and Germany, who follow the “relative effectiveness” model, and the United Kingdom (UK), which uses the “cost/QALY” approach.

In the UK, HTA is coordinated by NICE, which follows a clear, inclusive and timely process. There is ample opportunity for broad stakeholder input, an appeal process, timelines are defined, and there are clear consultation steps. Decision making is based on the ICER of a new technology being below a pre-specified threshold (£20,000-£30,000/QALY), or below £50,000/QALY for medicines that meet strict “end of life” criteria.

In the German “relative effectiveness” HTA model, there is clear separation between the assessment part of the HTA, performed by the Institute for Quality and Efficiency in Healthcare (IQWIG), and the appraisal step, conducted by the Federal Joint Committee (G-BA). At the assessment stage, IQWIG reviews the evidence and decides on the added benefit of the new technology, which is expressed on a six point scale, ranging from “reduced benefit” to “major benefit” compared with the current standard of care. In France, the added benefit of the new technology is rated on a five-point scale of “Improvement of Medical Benefit” (ASMR), with an ASMR rating of I showing major improvement (e.g. demonstrated effect on mortality in a severe disease) and an ASMR rating of V showing no improvement versus standard of care. The Haute Autorité de Sante (HAS) assesses the evidence, whilst the pricing and reimbursement decision is the responsibility of the Commission de Transparence (Transparency Commission).

**Industry perspective**

**Key elements of an effective HTA system**

A number of models of HTA have evolved across different European countries over the last twenty years. Pharmaceutical companies need to navigate these different systems and different value assessment criteria in order to ensure patient access to new medicines. These different systems can result in diverse coverage decisions for the same medicine, based on the same evidence package. Our perspective is that there are examples of good practice in a number of systems, but that none of the existing HTA systems are ideal. For this reason, we have identified the key elements of an HTA system that would balance the needs of payers, healthcare professionals, patients and industry. Over the last decade there have been several publications by academics and international forums outlining key principles for HTA (Drummond et al, 2008; EUPATI, 2015), regarding the structure and methods of HTA, the process for conducting HTA, and the impact of HTA on decision-making. As a major stakeholder in HTA, industry needs to be confident that the key principles around allocation of healthcare resources provide an opportunity for flexible dialogue between industry and decision-makers within the relevant agencies. To achieve this dialogue, the key elements of an effective HTA system from an industry perspective include transparency, stakeholder engagement, independence of HTA assessment bodies and payers, accountability, a locally relevant scope and an appropriate evidence framework (Figure 2).

HTA and the associated decision making processes should be founded on principles of fairness, evidence-based decision-making and transparency. The lines of communication between all stakeholders and organisations involved should be clear. Transparency is necessary to understand the criteria used, the analyses conducted and the reasons for the recommendations or restrictions. However, commercial-in-confidence data need to be protected and respected.
HTA should actively and formally engage all stakeholders at key stages of the process, including scoping, submission, consultation, assessment and appraisal. Following the evidence assessment, it is important that the process enables dialogue between decision-makers and industry, in order to discuss the value assessment, as well as pricing and access arrangements. In our experience, systems that enable on-going dialogue and are flexible in co-creating pricing and access arrangements facilitate patient access to modern medicines. Negotiation is a key part of the process in Spain and Italy for example, where patient access benefits from industry’s involvement in pricing discussions following the reimbursement decisions.

Assessors, decision-makers and payers should be independent from each other. In addition, clear conflict of interest policies are required to protect the independence of HTAs.

HTA should be a time-limited process with clear accountability. For example, the HTA process in the UK is specified to take 39 weeks from scoping consultation to publication. All stakeholders, including industry and academic groups, should be accountable to decision makers for the evidence they provide. Decision-makers can then be accountable for access decisions made.

HTAs should be locally applicable, i.e. not directly translated “verbatim” across borders. Differences in the standard of care between countries lead to differences in the relative effectiveness of a treatment, and this needs to be accounted for. The level of a country’s organisational sophistication also needs to be considered when adopting the approach of a more developed country.

Finally, an efficient HTA system should have all appropriate evidence included in a value framework that reflects the unmet needs of patients and clinicians, and should consider the feasibility of sourcing all the evidence supporting the value of the intervention in the relevant jurisdiction. The NICE approach may not be suitable for many countries where evidence around resource use and outcomes to inform QALY assessments would be easy to quantify.

From an industry perspective, the opportunity for on-going dialogue during the appraisal process, combined with a solution-focussed, flexible, pragmatic approach will encourage a more efficient HTA process and ultimately optimise patient access to new and innovative treatment options. As the use of Patient Access Schemes (PAS) increases in Europe, a willingness to explore confidential patient access schemes is now even more important, including innovative contracting or financial risk sharing options. Currently, existing PAS can be classified broadly as either performance-based or finance-based. PAS can be applicable either at patient- or population- level, although in practice schemes may combine elements from both performance and finance systems (Figure 3).

It is important to note that HTAs typically assess the value of new technologies rather than the affordability of introducing them. As evaluating affordability is more a remit of payers than HTAs, additional mechanisms are needed to manage this in national jurisdictions. PAS, such as risk sharing, confidential discounts or price capping, can be used to address potential affordability issues that are a concern of payers. These are often managed through confidential agreements, to protect both parties from unintended and unwarranted arbitrage.

In the UK, NICE coordinates the HTA process, while currently, through a five year (2014-2018) voluntary agreement, the Pharmaceutical Price Regulation Scheme (PPRS) facilitates managed market entry and influences affordability of new and improved medicines by controlling the prices of branded drugs sold to the NHS. Prices are negotiated between the Department of Health (acting on behalf of the UK government) and the branded pharmaceutical companies (through the Association of the British Pharmaceutical Industry [ABPI]). In addition, NICE is permitted to consider PAS that are pre-approved by Government Ministers and Department of Health is the appraisal process. This provide manufacturers with more flexibility by which to meet the cost per QALY thresholds set out by NICE.
QALYs and cancer interventions

Cost per QALY (CPQ) analyses are complex and subject to uncertainty. They rely on synthesis of evidence from a diverse range of sources and require the use of complex statistical techniques to model the costs and outcomes over long periods of time. In addition, utility measures that are used to capture health benefits are notoriously insensitive and frequently fail to recognise important elements of patient well-being. For these reasons, CPQ methodologies can be problematic, which is most apparent in the field of oncology.

A recent study supports this view (IMS, 2015). In a study conducted in 2015, the IMS Institute for healthcare informatics examined the approaches to and implications of reimbursement for nine new cancer drugs in countries adopting a CPQ HTA model, compared with those not considering the CPQ assessment. The research showed that patients in the five countries where CPQ was the basis of the country’s HTA model had less access to cancer medicines than patients in countries who had HTA systems based on relative effectiveness assessment (IMS 2015). Where CPQ was assessed, fewer new cancer drugs were reimbursed (Figure 4), with longer reimbursement decisions timelines. In contrast, access to new non cancer drugs was comparable across the countries studied. The data also showed lower cancer survival rates in those countries adopting a CPQ methodology, particularly the UK. Countries adopting CPQ based HTA appear to achieve less value and benefit for patients. This report suggests that systems with a rigid approach for economic evaluation, such as those using a CPQ HTA model, have access to fewer new oncology treatments.

Discussion

A good starting point for countries considering implementing a nationally relevant, rational and affordable HTA system would be to follow the key principles listed in this article (Figure 2). There is a legitimate case for payers, physicians, patients and decision makers to scientifically assess the value of healthcare technologies to ensure the most efficient use of available resources. HTA systems should be strongly patient focused and built on a system that enables dialogue between industry and the payer. Our view is that a system built around openness and pragmatism will generate better outcomes and access for patients in specific jurisdictions.

The design of a new HTA system will have a major impact on patient access to new and innovative medicines. A system that values new therapies on the basis of clinical benefit and subsequently enters a negotiation period (where companies work with the payers to determine how to deliver these medicines affordably), potentially leads to better outcomes for patients compared with systems driven by rigid cost-effectiveness thresholds.

The World Health Organization (WHO) recently undertook a global survey on the use of HTA (WHO 2015). Countries were classified as either low, middle or high income as classified by the World Bank. A section of the survey asked about the utilisation of HTA in public sector decision making. Results showed that all low income and the majority of the middle income countries use HTA for planning and budgeting, whereas high income countries are more likely to use HTA to determine reimbursement status or inclusion of a technology in a benefit package. Additionally, low income countries reported most use of HTA for population level health interventions, whereas high income countries were more likely to use HTA to determine access to specific technologies aimed to supplement the existing comprehensive coverage, such as new medicines or devices. This fundamental difference in questions being addressed by HTA and difference in decisions being informed confirms that it is not appropriate to simply “cut and paste” methodologies from established HTA systems to developing ones; methods may not be directly transferable. The survey also questioned the structure of HTA organisations in the countries: two thirds of
the countries reported a national organisation, department or unit that produced HTA reports for the Ministry of Health. The proportion was highest in the European and American regions (over 80%) and lowest in the African region (33%). The report also demonstrated a high variation in available resources, with 15 countries having 5 or fewer professional HTA staff whilst 5 countries have more than 100 (individual country or region data was not available). Additionally, across all countries a lack of qualified human resource was reported as the main barrier to producing HTA for use in decision making, followed by budget and information (i.e. data). Fewer than half of the countries had any academic or training programme to build capacity. The report does not make recommendations as to what “good” should look like, but simply concludes that the WHO will continue to advocate and raise awareness and promote the use of HTA to inform decision making. Overall this report emphasises the need for any “new” system to be fit for purpose, pragmatic in its expectations and not expected to match up to resources of some well-established agencies.

At the European level, a relatively new initiative by EUnetHTA is in the process of creating an effective and sustainable network for HTA across Europe. It aims to support collaboration between European HTA organisations, to bring added value at the European national and regional levels through facilitating efficient use of available resources for HTA, creating a sustainable system of HTA knowledge sharing, and promoting good practice in HTA methods and processes (EUnetHTA 2015). It is however premature to adjudge this European centralised initiative as it is yet to demonstrate it can have meaningful impact on process efficiency or patient access. Griffin et al (2015) reported on their experience of five EUnetHTA pilots to evaluate the ability of partners to collaborate on relative effectiveness assessments across pharmaceuticals and medical devices. The pilots demonstrated that EUnetHTA partners can collaborate on relative effectiveness assessment reports; however, the EUnetHTA needs to deliver efficiency gains across the HTA process in order to retain the support of company boards for future relative effectiveness assessments (Griffin et al, 2015)

**Conclusions**

There is no single “right” HTA model, but good practice elements exist across different systems in Europe and other countries such as Canada and Australia. Key aspects of any new HTA system must include stakeholder engagement, transparency, timely process, accountability and clarity around HTA decisions. Medicines should be reimbursed according to their added value defined as meaningful improvement in patient-relevant clinical outcomes versus current standard of care; HTA should not define value predominantly in terms of CPQ. Our view is that many current HTA systems suffer from complexity, lack of transparency and limited focus to patients. Mechanisms that allow flexible contracting solutions and risk sharing models can help address potential affordability concerns. Finally, respect for commercial in confidence arrangements is key to protecting long term drug development and enabling innovation.

In conclusion, it needs to be recognised that although sharing HTA experience across countries is beneficial decisions based on HTA needs to remain a national responsibility. HTA should adhere to appropriate methodological standards with its process complying with rules of good governance, including transparency and stakeholder involvement, but also be relevant and appropriate for the level of national resources capabilities and capacity. Countries who are considering introducing HTA need to define processes that reflect national competence and address local priorities.

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