Abstract
Over the past ten years, health technology assessment (HTA) has become an increasingly prevalent evaluation in the route to market for new medicines. Planning for success in HTA reviews should therefore be an integral part of a product development strategy to reduce time and risk in getting new medicines (or other health technologies) to market. As HTA becomes more broadly applied, both across countries and beyond medicines to other healthcare technologies, the methodologies and policies driving it need to be assessed to ensure it remains fit for purpose.

Health technology assessment (HTA) is playing an increasing role in determining which medical technologies are made available to patients throughout Europe. Regulatory authorities have a formal role, defined in law, to determine whether a health technology, such as a pharmaceutical medicine, medical device, or diagnostic test is safe, effective and of high quality. However, HTA agencies, such as the National Institute for Health and Clinical Excellence (NICE) in the UK and the Institute for Quality and Efficiency in Healthcare (IQWIG) in Germany, focus on evaluating whether a health technology offers value for money, and are becoming increasingly dominant as the final gatekeepers in determining which technologies are and are not used in routine patient care.

Access to many European markets, post regulatory approval, is controlled or influenced by HTA agencies, whose decisions depend heavily on value arguments, informed by evidence on relative benefits compared with existing standards of care, and economic modelling. While the regulatory decision to approve or not is based on a scientific judgement, the HTA decision – which fundamentally results in a technology either being reimbursed (or funded) or not – is a value judgement, albeit based on scientific evidence. This has many implications for medical technology companies, whether in the pharmaceutical, device or diagnostic business.

The intention of healthcare services (eg, the UK’s National Health Service) that use HTA is for it to help inform the best use of scarce resources. Manufacturers of innovative products that keep this consideration at the forefront of their development plans can therefore use it to their advantage. When developing a new technology such as a medicine, companies that ensure appropriate evidence is generated, which address both the regulatory requirements and the concerns of reimbursement/HTA agencies, are more likely to benefit from faster adoption of their products. This in turn ensures a sustainable business model, whereby revenues from a successful product launch are then available to finance the next innovative product in the pipeline.

There are issues though. While regulatory requirements are clearly defined, and harmonised within Europe both for drugs and devices, HTA requirements are not. Different HTA agencies will accept varying degrees of evidence; their processes are individual, as are their value systems. For example, IQWIG in Germany states it strongly favours evidence from randomised controlled trials (RCTs), whereas NICE states it will consider any relevant evidence, such as registry, cohort or observational data, as long as it can be demonstrated to be reliable. Indeed there are examples where a positive NICE decision has rested on non-RCT evidence.

Different decisions on the same body of evidence
An additional consideration for manufacturers to address is that different healthcare systems have different interpretations on what constitutes “value”. This can mean that the same data can be reviewed by different healthcare systems which then come up with, legitimately, different decisions.

For example, the French system first defines an “improvement in medical benefit”, the ‘ASMR’ (Amélioration du Service Médical Rendu) rating for the technology, which determines the degree of added clinical value compared with the current standard of care. The ASMR rating (on a scale of 1 to 5) then determines the value, or price premium, the healthcare system is willing to pay for the product. This differs from the UK’s NICE system, which is based on a £/QALY system (“cost per quality-adjusted life year”). Here the value of implementing a new technology is based on the ratio of difference in cost, divided by the difference in outcomes (measured in QALYs) to change from the existing standard of care to the new technology. In this system an improvement in outcomes also justifies a higher cost but, unlike the French system, the cost equation also takes into consideration any increases (or decreases) in delivering care along with the cost of the new technology (such as the cost of delivery, length of stay, concomitant medications, etc). Factoring this in to a product development strategy plan means that teams need to be able to assess market by market the likely interpretation of the value of a new
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technology’s benefit when planning their market access strategies, recognising that what is optimal for one market may not be optimal, or indeed positive, in another.

Potentially more of an issue though is the variation in HTA processes. Some markets (such as Scotland and France) review all new technologies, especially drugs, whereas others (England) are selective. Some HTA processes are initiated by the manufacturer, and therefore the manufacturer has a degree of control over the timing (such as in France), whereas others are initiated by the HTA agency (Germany and England).

Positive attributes of a good HTA process
Several key themes are generally accepted as positive attributes of a good HTA process. These include:

- Broad stakeholder involvement, including industry, clinicians and patient groups, all with the ability to contribute evidence to the process
- Transparency in the process, with clearly marked timelines and decision points
- Transparency in the methodology, both in evidence included, types of analysis and the decision-making criteria
- Decision-making should be from a societal perspective, including all costs and benefits of a technology, not just those confined directly within the healthcare system. (Such costs and benefits may include patient out-of-pocket expenses, differences in productivity or the impact of treatment and patient benefits on family and caregivers.)

A good R&D development plan will prepare for market access from the beginning, addressing both the regulatory and reimbursement or HTA requirements. However, as can been seen from some of the issues raised here, the HTA arena is less consistent than the regulatory environment. There have therefore been calls to improve the efficiency of the reimbursement process, reducing duplication between markets, and the time taken in some markets to reach a reimbursement decision. While this desire sounds laudable, there are still many issues that need to be addressed.

Local responsibility for healthcare decisions
Healthcare systems maintain rightly that decisions on healthcare provision are local responsibilities, not something that can be centralised like regulatory decisions. Countries are at different stages of economic development, have structurally different healthcare systems, and may value different types of benefits or outcomes. Imposing a centrally mandated one-size-fits-all reimbursement system is therefore not feasible.

The goal of reducing duplication of evidence synthesis and analysis, and sharing of knowledge, may sound like a more pragmatic objective. Indeed, this view is supported by many, including the EU Joint Action programme ‘EUnetHTA’, which includes as part of its mission ‘creating sustainable systems for knowledge sharing and provision of tools to assist the production of HTA in European countries by allowing HTA information to be shared and adapted, thus supporting processes and enhancing efficiency in HTA at the country level’. Only time will tell how successful this will be.

While a coordinated approach to evidence-sharing may help developing markets that have little resource or experience in HTA to undertake evaluations, it is unlikely to benefit larger markets with established HTA systems. One attribute of many systems, and probably most transparently at NICE, is the debate, analysis and re-analysis of different scenarios that occurs during the appraisal process. If the effectiveness data are supplied by a third party, for example if IQWIG reviewed a technology first, and made its data available through the EUnetHTA network to reduce duplication in other countries, or the EMA expands European public assessment reports (EPARs) to include information on relative efficacy, then those datasets need to be the right ‘cut’ of subgroup, endpoint, follow-up, and inclusion/exclusion criteria for that analytical work not to be repeated locally by other HTA agencies. This is rarely the case, and so the potential value of a “core HTA” that contributes to local decisions in each healthcare system will need to be demonstrated before it is likely to be widely adopted.

A final thought for consideration is how HTA is applied across the different types of healthcare technologies, beyond pharmaceuticals. While pharmaceutical companies have been dealing with HTA evaluations for many years, it is increasingly now being used to evaluate a wide range of medical devices, surgical procedures and other healthcare interventions. Existing HTA methodology has developed, explicitly or implicitly, to evaluate drugs. The regulatory environment, and the intellectual property (IP) rights afforded to drugs, facilitate the generation of evidence both pre- and post-launch that has supported HTA decision-making. The three factors: regulation, reimbursement and IP protection are not necessarily in conflict. A different situation exists, however, with medical devices.

Assessment for medical devices?
The same HTA methodologies are now being applied to all medical technologies. On one hand this makes sense; an intervention is an intervention, and it is possible for a physician to have to decide between treatment options of either a drug or a procedure, so why would you have different hurdles for HTA decision-making? On the other hand, the regulatory process for medical devices is very different, requiring varying degrees of evidence, reflecting the different risk–benefit ratios between, for example, a walking frame and an implantable defibrillator. Medical devices also do not benefit from any data exclusivity periods like drugs, so a product’s lifecycle can be typically less than two years, and competition is normally rapid and numerous. For an HTA process to then impose pharmaceutical-like expectations or requirements in terms of evidence, irrespective of cost, expected lifecycle, or ability to generate evidence at any given time point, lacks a recognition of the healthcare market it is trying to inform. If HTA is to be more consistently and routinely applied to medical devices, then the methods applied need to adapt, or the procurement environment needs to evolve to incentivise greater evidence generation.

Conclusion
HTA is here to stay, and industry is gradually adapting to its requirements. It is right that any technology should demonstrate its value if the aim is for it to be successful. Given most markets are ‘centralised’ healthcare systems, where a body is making decisions on behalf of a population, those value decisions need to be transparent. The processes by which they are made and the evidence demanded also need to be proportionate to the size of the technology, and not undermine its sustainability.

Note on the author
Adrian Griffin is a NICE technology appraisal committee member.