Marketing pharmaceuticals in the 21st Century poses a number of new challenges, one of which is the growing need to provide value-for-money arguments for healthcare interventions. Health Technology Assessment (HTA) groups, such as NICE and the SMC, now play a key role in the market access of new products. This article provides practical steps to enable teams to maximise the outcome of HTA submissions, based on the experience of Abacus International, who has made over 60 submissions.

A practical guide by Ruairi O'Donnell and Christie Niziol
1. PLAN AHEAD
Rejection from HTA groups prevents formulary inclusion and product uptake. Restricted recommendations influence product positioning and limit sales potential. HTA endorsement is an opportunity to be exploited on a global scale, particularly if a product is given a first-line position. In order to do this, successful HTA submissions require foresight and careful planning. Leaving preparation to the last minute invariably leads to data gaps, unexplored modelling options, incomplete adherence to guidance from HTA agencies, and increased potential for error. The ultimate in forward planning is to develop clinical trial programmes that compare the new product with the ‘gold standard’ therapy. In order to provide a valid cost-effectiveness argument, appropriate economic and humanistic data need to be collected.

Conducting a gap analysis at least 12 months before a submission deadline provides an opportunity to fill the evidence gap. Section three describes options for filling data gaps not resolved by primary trial data.

The Department of Health instructs the National Institute for Health and Clinical Excellence (NICE) regarding treatments to be assessed based on one or more criteria: 1) does the treatment relate to a government health priority area?; 2) would it address a disease currently managed sub-optimally?; 3) would the treatment significantly improve patient health and quality of life (QoL)?; and 4) would issuing guidance have a ‘real’ impact on patient health and clinical practice? Applying these criteria gives a reasonable prediction of the likelihood of NICE appraisal. Many companies undertake health economic modelling and systematic reviews in preparation for launch. These data are utilised if a NICE submission is required, providing the analysis and evidence is in keeping with HTA guidance. Advisory boards designed to replicate an HTA team provide an early indication of whether NICE might endorse or reject a product.

The Scottish Medicines Consortium (SMC) assesses all new medicines, as well as any changes in licence. The SMC encourages submission of evidence at the time of product launch; therefore, working back from a product’s prospective launch date allows accurate planning of HTA resources in conjunction with post-launch marketing initiatives. Modified formulations of existing medicines may be suitable for abbreviated submissions. However, if you have any doubts about which submission is required, consult with the SMC early.

If you are using a third party to create the model and submission document, early planning is essential. Lack of clarity in project processes, timelines or agreed approaches can lead to late revisions and other sub-optimal circumstances – delaying submission.

2. OBTAIN EXTERNAL CLINICAL INPUT
Recruiting external clinician input at an early stage can provide benefits before, during and after the HTA process.

In preparation for an HTA submission, assessment of current clinical practice is very important. Choice of an inappropriate comparator is a common reason for rejection of an SMC submission and/or poor critique of a NICE submission. The ‘gold standard’ treatment chosen for a pivotal clinical trial may not be relevant for a national HTA submission, especially if trials were conducted in other countries. Consultation with practising clinicians in the field/country of appraisal ensures that all appropriate comparators are considered and that current practice, treatment consequences and budget impact predictions are reliable. Moreover, expert panel meetings can be conducted to achieve consensus statements in the absence of robust clinical data.

Validating key messages with expert clinicians can enhance the robustness of arguments within HTA submissions. If possible, include a statement indicating which experts have validated the clinical and economic information. During implementation, clinicians can help ensure guidance is adhered to in local NHS settings. Enlisting key opinion leaders (KOLs) as lead authors on supporting publications will add considerable weight to the messages. Involving patient interest groups and charity organisations in the HTA consultation process has been shown to reduce the likelihood of restricted recommendations.

3. FILL DATA GAPS
Cost utility analyses, required by HTA assessors, need a measure of patient QoL. However, many clinical trial programmes do not include appropriate patient-reported outcomes (see section one). Disease-specific questionnaires are not suitable for HTA purposes. Generic measures, such as the short-form health survey-36 (SF-36) and the EuroQoL are preferred by HTA assessors as they facilitate decision making across different disease areas. If these data are not available, there are a number of data collection methods to consider.

Web-based clinician surveys provide essential utility and resource-use data in a short timeframe. If timelines are less of a constraint, population-based questionnaires can be conducted in conjunction with local GP practices or hospital populations. Existing patient record databases can also be incorporated into marketing strategies post-HTA (see section eight). Whilst less reliable than primary trial data, these approaches have been used to yield successful HTA endorsement as long as adequate sensitivity analysis is conducted (see section six).

Budget impact estimates form an integral part of any HTA submission, providing decision makers with an estimate of the likely economic impact of a new technology on resources. Prevalence and incidence data, as well as prescribing information, are commonly used in these calculations. In the absence of published estimates, patient record databases provide access to primary care data on diagnosis and treatment...
patterns. These large-scale databases may also identify unmet needs and additional market opportunities.

Often, HTAs require indirect comparisons between similar medicines. To do this effectively, a systematic review culminating in a robust meta-analysis of clinical endpoints may be required to produce meaningful data. Indeed, submissions including systematic reviews are less likely to be rejected by NICE.

4. ADHERE TO MOST RECENT HTA GUIDELINES
In the UK, both NICE and the SMC publish guidelines on their websites as to how manufacturers’ submissions should be completed. They stipulate the methodology required for economic evaluations, as well as how clinical evidence should be presented. They are regularly updated – it is vital to use the most up-to-date submission forms and guidance before commencing work. Signing up for newsletters and email alerts is an effective way of following changes in HTA processes.

5. BUILD THE ‘RIGHT’ MODEL
In the absence of post-marketing resource-use data, pharmacoeconomic models are routinely required for HTA submissions. These mathematical models, often built in Excel, combine health outcomes with healthcare resource-use costs. Where possible, models should reflect current clinical practice in the relevant location; careful consideration must be given to clinical and healthcare cost inputs.

Guidelines dictate the sources of healthcare costs, the perspective of the analysis, discount rates, type of sensitivity analysis, data presentation and model methodology. To give products the best chance of success, strict adherence to these guidelines is essential. For ease of assessment, models should be transparent and straightforward to use; even complex arguments should be presented simply and clearly. Do not assume that generic models created in different countries will be sufficient for submission to UK HTA boards.

In the UK, cost utility analyses are the approach of choice for HTA purposes. This analysis produces a generic measure of cost-effectiveness, the cost per quality-adjusted life year (QALY), which allows comparison of treatments across disease areas. Choosing not to undertake a cost utility analysis requires careful justification and should only be done following consultation with the HTA assessors.

Choosing the correct comparator for the economic evaluation is critical to a submission’s success. Cost-effectiveness is a relative concept, producing an incremental cost-effectiveness ratio (ICER) versus a comparator intervention. NICE defines the technologies to be compared during a scoping process. However, in Scotland, the choice of comparator is left to the manufacturer. SMC guidance dictates that the most appropriate comparator is that which will be displaced by the product being appraised; placebo is not usually a suitable option. Inappropriate choice of comparator is the main reason for SMC rejection (see section two).

6. DEAL WITH UNCERTAINTY
Pharmacoeconomic models are an approximation of clinical practice and the costs involved. For this reason, comprehensive sensitivity analyses investigating the impact of over/underestimation of variables are an important aspect of HTA submissions. Uncertainty among key parameters cannot go untested; failure to do so will be viewed with suspicion by reviewers and may contribute to negative recommendations. Both NICE and the SMC give specific instructions on the types of sensitivity analyses required.

7. SPREAD THE WORD
Positive guidance does not guarantee consistent product uptake. It is essential that local budget holders are aware of positive recommendations from NICE and the SMC. Ideally, they should be made aware of forthcoming guidance prior to publication, allowing them to plan for new interventions. Some companies produce newsletters or flyers regarding pending guidance; more commonly, a summary of the published guidance is produced and disseminated by mail or in person by the sales force. Workshops, advisory boards and local presentations can also be used, and the guidance can be alluded to in marketing materials.

8. SUPPORT YOUR CASE
In addition to disseminating HTA guidance, it is important to publish key data. HTA groups will find it difficult to base endorsement on information that is not in the public domain;
Therefore, it is advantageous to publish key trials promptly. Publishing health economic arguments in a peer-reviewed journal increases the perceived reliability of the methods in the submission. Similarly, any secondary studies conducted to fill data gaps (e.g., patient database studies and systematic reviews/meta-analyses) should also be published.

Other supporting messages may include the burden of disease and inadequacies of current management that support the need for new intervention. Such messages can be investigated through patient record databases, surveys and advisory board meetings. Journal articles and/or scaled-down posters also act as useful resources for the sales force.

9. AID LOCAL IMPLEMENTATION

When planning a NICE implementation campaign, it is important to consider Primary Care Trust (PCT) processes (see figure, page 3); guidance is disseminated to individuals within the PCT for implementation. Ensure maximum exposure of the important recommendations, possibly with a specific sales force campaign.

PCTs must interpret the guidance and estimate what it means to them. Which patients does it affect? How many patients are there and what is the likely budget impact? What other resources will the guidance impact (staffing, clinics, diagnostic equipment, etc.)? Support this process with high quality summaries of the evidence, local budget impact tools and business cases for funding requests.

Finally, the people who really bring about change, the prescribers, have to adopt the recommendations. Formularies need to be altered, patients must be identified and sometimes therapies need to be changed. Normal marketing and sales activities remain an important element in influencing change at this level.

Communication with KOLs is a good way to identify potential barriers to implementation before development of an HTA campaign. If budget is critical, then a budget impact calculator is important. Sometimes, the limiting factor may be identifying the recommended patient group; or, it may be access to diagnostic equipment, specialist clinics or even trained staff. The best way to overcome specific barriers is to identify them early.

10. AUDIT IMPLEMENTATION

An analysis of IMS primary and secondary care data between 2000 and 2003 found that NICE guidance has variable impact on prescribing practices. For instance, after NICE guidance on advanced colorectal cancer in March 2002, a sharp increase in use of oxaliplatin and irinotecan as first- and second-line treatments was observed. In contrast, the use of atypical antipsychotics appeared to be unaffected by issuing of guidance in June 2002.

Encouraging adherence following a NICE recommendation will influence sales. Audits and surveys allow uptake of guidance to be assessed. If detailed enough, PCTs can be benchmarked against one another. Surveys are useful for gathering information on level of agreement with recommendations, as well as identifying barriers to uptake. Ultimately, audits can provide evidence for future HTA submissions, so it is worthwhile reviewing audit recommendations in pre-existing guidance.

NICE is interested in the results of implementation surveys, and evidence of poor uptake of guidance provides useful material for discussion at national and local levels.

Company sales and marketing activities always remain an important element in influencing change at all levels.

Abacus International

Trying to access PCT decision-makers?

Our NICE implementation toolkits and audit services are just two ways in which Abacus can help.

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Reference

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