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Practical advice for Early Scientific Advice (ESA) in HTA submissions

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Practical recommendations on preparing for and implementing Early Scientific Advice (ESA) in HTA submissions

A step-by step guide on the benefits, processes, and key considerations involved in the Healthcare Technology Assessment (HTA) Early Scientific Advice (ESA) consultation as part of planning the holistic evidence generation to support the design of an asset.

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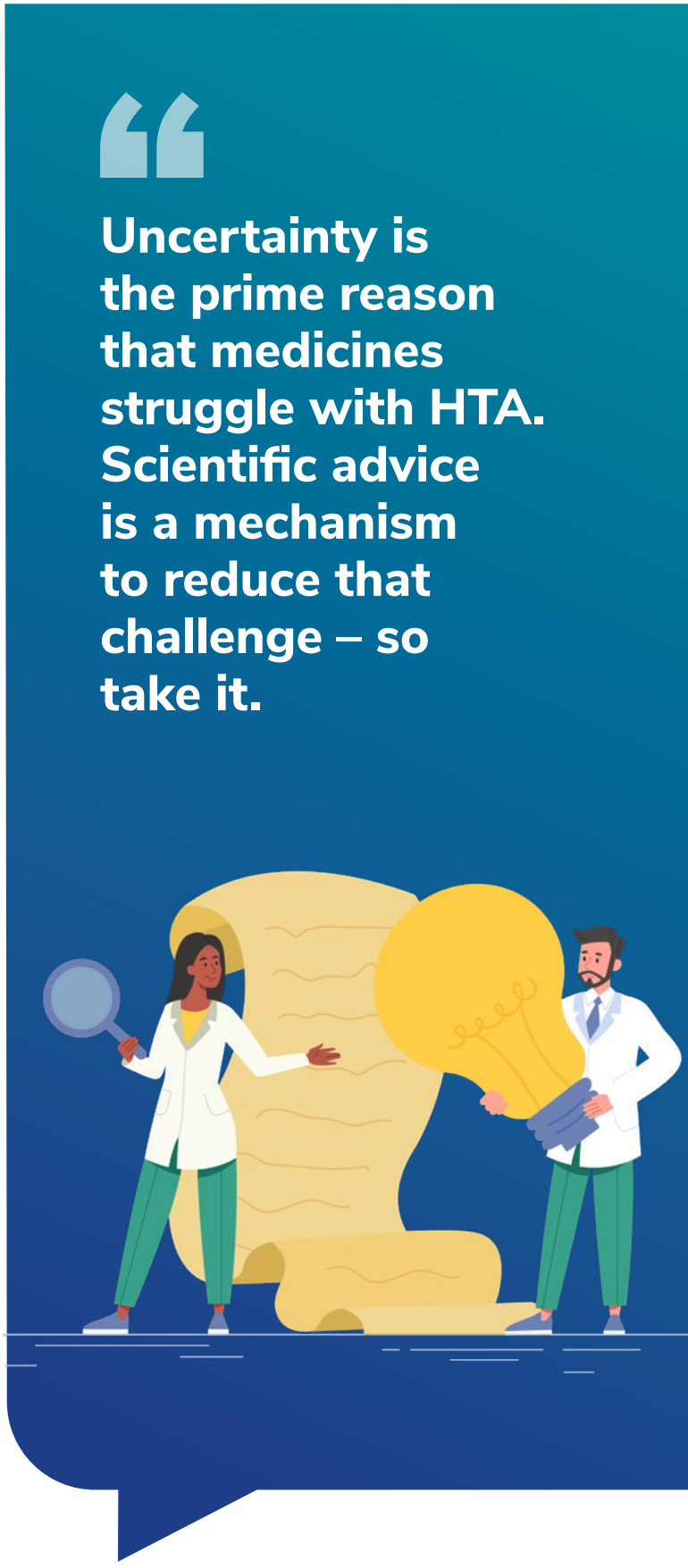
In recent years, the biopharma market has become progressively complex. As a result, payers are feeling increased pressure to make the right decisions based on the perceived value of each product. Payers must take into consideration not only the clinical efficacy of a drug, but also its safety profile, side effects, and cost-effectiveness, among other factors.

Health Technology Assessment (HTA) is an important tool for decision-makers when it comes to evaluating the clinical effectiveness and cost-effectiveness of new pharmaceutical products and services. There are several barriers that can negatively impact HTA and pricing outcomes, including uncertainty and trials that are not designed with the payers' evidence needs in mind.

HTA agencies can assist biopharma companies at the early stages of development to ensure they are meeting the expectations of payers. Specifically, HTA agencies offer opportunities to receive early scientific advice (ESA), which involves discussions around key topics such as clinical development programs, economic analyses, and evidencegeneration plans. The implementation of the resulting recommendations can reduce payer uncertainty and lead to optimized HTA submissions.

According to Ross Selby, Head of Global Patient Access at Takeda Oncology via NICE: "Uncertainty is the prime reason that medicines struggle with HTA. Scientific advice is a mechanism to reduce that challenge – so take it."

ESA involves engaging regulatory and/or HTA agencies to provide early-stage feedback on an asset's clinical development program. While seeking advice from regulators is more common for biopharmaceutical companies, many miss out on the opportunity to speak to payers. The advice can be used to avoid HTA challenges and is confidential and non-binding. However, ESA cannot include feedback on ongoing trials and does not predict the outcome of future HTA appraisals. It is also important to note that ESA cannot include pricing discussions. There are two main types of ESA: HTA agency consultation (involving a single agency) and joint-scientific advice (involving multiple agencies).



Common topics for ESA discussion

The early feedback provided in ESA engagements can save time and money by helping avoid decisions that might later result in unfavorable HTA or pricing outcomes. Some of the most common topics covered in ESA discussions include trial-design optimization, evidence-based value demonstration, payer expectations, design of network meta-analyses, and economic models.

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Trial-design optimization

The design of a clinical trial is crucial to the successful demonstration of value. All too often, manufacturers attempt to get to market as quickly as possible and rush into trials without ensuring they have a robust understanding of stakeholders' evidence requirements, including those of the payer. This can lead to problems down the line as HTA committees are likely to identify issues with the trial design and overall evidence generation that could have been avoided. Failing to consider the payer during the design of clinical trials can be particularly detrimental in disease areas with significant unmet needs such as rare diseases, oncology, and targets for cell and gene therapies. In these cases, the regulator often requires less evidence to speed up the patient's ability to access life-changing treatments. However, payers often require more robust evidence than the results gleaned from Phase 2 single-arm studies or placebo-controlled Phase 3 studies.

Actioning these evidence requirements in the clinical development program can, however, result in extending timelines to regulatory approval and increasing the costs of clinical development plans.

To mitigate this, manufacturers should take the time to identify all potential concerns that could be raised by HTA committees and the appropriate approaches to meet payer evidence needs, while balancing these with the desire to ensure patients gain access to valuable new treatment options with minimal delay. This includes considering everything from primary and secondary outcomes to the enrolled population and the comparator arm.

Understanding payer expectations

It's crucial for manufacturers to fully understand the expectations of the payers in each market. Early consideration of the payer's perspective can help manufacturers make strategic decisions and create evidence packages that are appropriate for each region to optimize successful HTA outcomes and patient access to new therapeutic options.

ESA can involve the discussion of prevalent development issues such as the clinical trial design, relevance of the proposed trial comparator, choice of clinical and health-related quality of life endpoints, relevance of surrogate endpoints, and identification of eligible populations. Other common issues that may be discussed include the contribution of combination components, sample size, generalizability of enrollment criteria to clinical practice, the suitability of a modeling approach, and strategies to reduce uncertainty and help achieve a more acceptable incremental cost-effectiveness ratio.

ESA in practice

The development of submission materials for an ESA consultation can be a complex and involved process, requiring coordination between global and affiliate organizations. To ensure all stakeholders are adequately represented, it's essential to develop a clear and concise submission plan. This should identify the key points that need to be addressed as well as the specific roles of each organization. The plan should also allow for flexibility to accommodate changes that may arise during the consultation. These steps ensure the submission materials are comprehensive and accurate, and that the organization's interests are properly represented.

While ESA pathways can differ, they follow the same general route. Prior to the official start of the ESA process is the pre-submission phase. This includes the initial contact, request for ESA, scoping of the ESA, submission of draft materials, and agency feedback. The official start of the ESA process is signalled by the final materials submission. Then a face-to-face or virtual consultation takes place before the agency delivers its finalized response. An optional step includes the opportunity to clarify details of the final advice. The lead time for ESA engagements following materials' submission varies between HTA agencies and can take between 10 to 24 weeks.

Markets differ in terms of how feasible it is to request ESA for an asset. For example, in France, the asset must have a novel mechanism of action in the disease area and target an unmet need to be eligible for ESA. The early dialogue must also be finalized before the pivotal clinical trial begins. However, in the UK, NICE takes a more flexible approach, explaining that the optimum time to seek guidance varies by product but recommending manufacturers seek advice during the design of the registration study.[2]

Other markets deem products ineligible for ESA if the asset is a generic or biosimilar. There are also restrictions on joint-scientific advice and the landscape here is changing. In September 2021, the European Health and Digital Executive Agency (HaDEA) initiated EUnetHTA 21. This European Union (EU) initiative involves Joint Scientific Consultations (JSCs) which facilitate exchanges between applicants and HTA agencies early in the development process.

Taking a systematic approach

The Policy, Access, Value, and Evidence (PAVE) team at Fishawack Health has provided support to past clients throughout the ESA process. Some key activities conducted by the team include developing briefing books which outline the issues to be discussed, holding mock meetings to prepare for the real consultations, and attending and reporting on the ESA meetings.

Through this experience, team members have developed a sound understanding of the nuances of the process and how clients can best prepare for consultation meetings, culminating in the following best practices:

1. Plan in advance

Assess the feasibility of securing ESA in advance of key decision-making milestones. Note that some HTA agencies have waiting lists as long as 12 months, so plan accordingly and be clear on your goals for the ESA process, including mapping out the exact advice you require.

2. Create a briefing book

A briefing book sets the scene for the discussion and ensures you remain tightly focused on your goals for ESA. Ideally, creation of the briefing book should begin at least 2 or 3 months in advance of the consultation. The document should remain factual, focused on the claims you can legitimately make now, and include the aspirational profile, rather than specific value messages. While the briefing book will differ depending on the market, if you intend to enter multiple markets, it makes sense to start with a central briefing book that can be adapted.

3. Identify the main internal stakeholders

Having the right players involved in the ESA process is vital to its success. Subject matter experts from key areas such as clinical and statistics should be involved from the outset.

4. Prepare thoroughly

It's important not to waste time or effort during the meeting with details that can be planned for in advance. For example, you should prepare for any questions that are likely to arise and be equipped to take key meeting minutes. Conducting a mock meeting will align the team on who will answer each question, the responses to give, and provide insight into the questions the agency could ask. This ensures you have agreed on a clear position in advance and will provide well thought-through responses.

5. Include a debriefing step

A debrief should take place immediately after the meeting to ensure that all internal stakeholders are aligned on the next steps. You should also assign one or two attendees to prepare detailed meetings minutes.

6. Review advice cross-functionally

Once a written response is provided by the HTA agency, there will be a need for cross-functional clarification on implementing that advice. This collaborative review should be scheduled as soon as possible.

7. Leverage and share the insights

Once you receive the advice, incorporate the insights back into your plans. Part of the value of ESA is in helping raise awareness of the payers' evidence needs and managing internal stakeholder expectations, so make sure any decisions are shared with the cross-functional team.

Partnering with market access experts can make these steps seamless and ensure an optimal outcome of the ESA process, saving time and money by gaining support navigating each stage, and by gaining reassurance that the team is not missing crucial tasks.

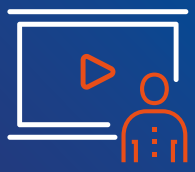
ESA support can lead to a Successful HTA submission

As the biopharmaceutical industry continues to evolve, companies need to be aware of the benefits that HTA agencies can offer. They can play a critical role early in the development of new pharmaceuticals by offering ESA. Common topics discussed include trial design, value demonstration, and payer expectations. The resulting advice can help biopharmaceutical companies meet the expectations of payers, which can lead to optimized HTA submissions and increased uptake of new therapies.

For the ESA consulting process to be as successful as possible, the manufacturer needs to plan ahead, ensure key stakeholders are involved, and take the appropriate post-meeting actions, including debriefing and cross-functional collaboration. Leveraging the experience of a consulting firm can help realize the full value of the HTA's ESA.

Get in touch

Contact us to find out how we can support you from pipeline asset to commercialization.



Watch the webinar

Hosted by PRMA Consulting (part of Fishawack Health) for more information and insights on the ESA process.

References

1. Haute Autorité de Santé, Evaluate Health Technologies: Guidance for national early dialogues on medicinal products, 2020. Accessed September 2022.
2. National Institute of Health and Care Excellence, Scientific Advice. Accessed September 2022.