

Early Engagement with HTA Bodies



- Early dialogue/scientific advice from health technology assessment bodies (HTABs) is an opportunity to increase the probability of obtaining timely reimbursement at the target price in the appropriate patient population by generating the appropriate evidence.

Scientific advice from regulatory agencies has been standard practice for a number of years; advice from HTABs, also known as early dialogue, is a relatively new offering and has a number of differences. It is recommended to seek HTA advice prior to initiation of Phase III or pivotal trials.

ADVICE FROM HTABs

Early dialogue is the process by which developers of new healthcare technologies can interact and ask insights/feedback from health technology assessment bodies on the clinical development programme strategies (i.e. planned confirmatory trial(s) and the economic rationale). The advice is prospective in nature and can be requested during the initial clinical development phase of the technology (i.e. during phase II to discuss the content of the planned phase III).

SCIENTIFIC ADVICE ON THE CLINICAL DEVELOPMENT PROGRAM

ADVICE FROM REGULATORS

Scientific advice is when a regulatory agency gives advice to a company on the appropriate tests and studies in the development of a technology. This is designed to facilitate the development and availability of high-quality, effective and acceptably safe medicines, for the benefit of patients. Advice can be requested at any stage of development of a medicine.

	HTAB	REGULATOR
Advice reduces the risk of generating inadequate evidence	✓	✓
Advice is legally binding	✗	✗
Advice given is considered as part of final HTA/regulatory assessment	✗*	✓

* Except in Germany, where G-BA advice feeds into the HTA process. Source: European Medicines Agency (EMA) and EUnetHTA webpages

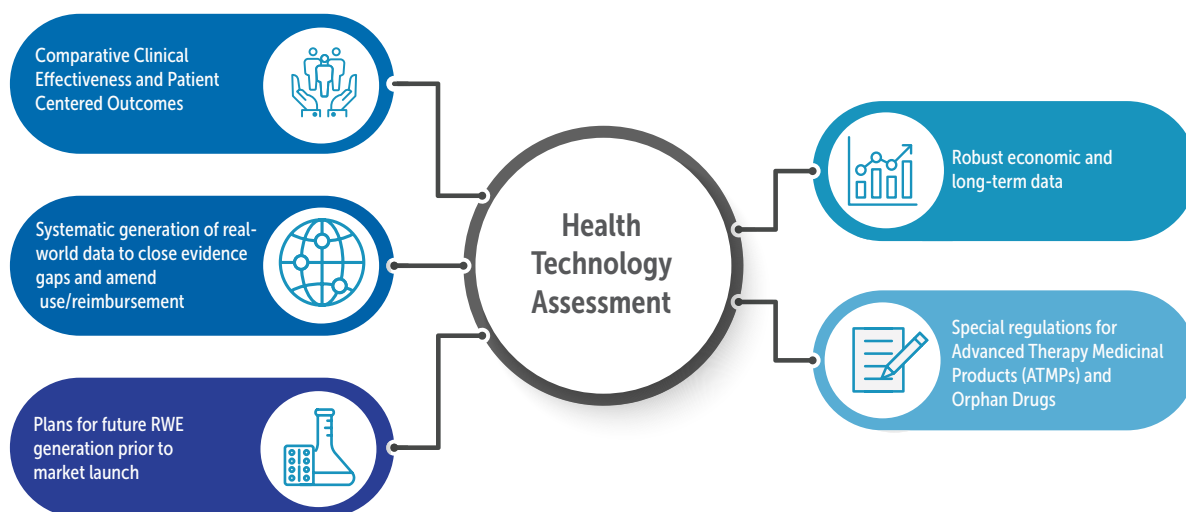
Early HTA and Parallel Engagement Strategy

Several pathways exist to early engagement with health authorities. Parallel EMA-HTA consultations are offered through a joint collaboration between EMA and EUnetHTA. Similarly a joint process is available through multi-HTA Early Dialogues facilitated by EUnetHTA or joint advice with NICE (UK) and CADTH (Canada). Early advice can be obtained by national HTA bodies such as HAS (France), G-BA (Germany), AIFA (Italy), NICE (UK) etc. Certara Evidence and Access offers strategic guidance and step-by-step support from the initial considerations of seeking early dialogue, planning the approach, developing the appropriate documentation and advising on next steps upon receipt of guidance. Compared with regulatory agencies, HTA bodies have different mandates and methodologies and are focused on understanding the value and consequences of making a new treatment available, including how it will perform in the real world, its economics, and impact within the local organizational and social context. Early HTA engagement has become a vital part of market access strategy and planning.

What should be considered when seeking advice? Some key questions are:

- Multi-HTA or national engagement?
- Risks in seeking advice?
- Timing?
- Willingness to follow advice?
- Financial implications?
- Ready for real world evidence generation plan?
- Ready for early economic modelling plan?
- Ready for early value proposition?
- Impact on MA/reimbursement strategy?

The need for better alignment between evidence generation strategy and HTABs' requirements calls for early engagement



Certara's Experience and Expertise



Certara has an in-depth knowledge and demonstrated expertise in engaging with HTA and regulatory bodies including strategic guidance to our clients on appropriate reimbursement issues as well as the development of respective submission documents and participation in related discussions.



Current members of our staff have worked for over 15 years in the field of HTA and some held positions in HTA agencies such as CADTH, INESSS, and DrugPlans, thereby bringing the direct payer perspective to projects.

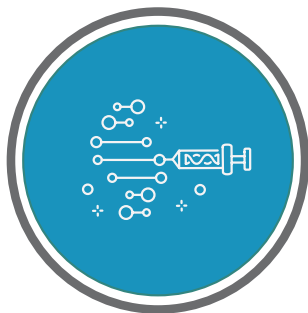
STRATEGIC CONSIDERATIONS

The collage shows various strategic planning documents. Key elements include:

- ons and Applicant's position:** Lists questions on Chemical, Pharmaceutical, Biological, and Toxic-Pharmacological development.
- Evidence Gaps:** A diagram showing gaps in evidence between different stages of development.
- Company position & rationale:** A diagram showing primary, secondary, and tertiary prevention strategies.
- Value Proposition:** A diagram showing the relationship between clinical and commercial success.
- Early economic model / RWE plan:** A diagram showing the development of a Real-World Evidence (RWE) plan to address evidence gaps.

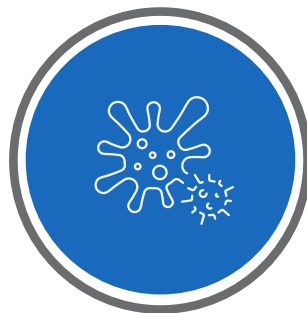
We have provided tactical support to our clients by developing the required documentation including the value proposition, questions and rationale and modeling plans in a number of therapeutic areas including gene therapy, rare and orphan indications in hepatology, oncology, hematology and infectious disease.

Certara Case Examples



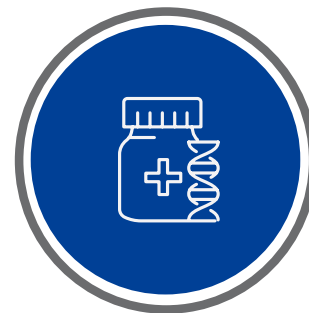
Gene therapy impacting treatment paradigm and an innovative trial design

Acceptance of secondary endpoints and validity of PRO tools and questions whether HTA bodies would consider RW data generated after the time of regulatory filing as valid evidence in the assessment in a context of changing market dynamics. Following engagement, endpoints were confirmed and study duration extended.



ATMP used in the acute management of the exacerbation of a chronic disease

Given the nature of the disease, Sponsor wanted to validate that the study duration was appropriate. Substantial differences in the management of the disease across countries posed challenges in terms of analysis and interpretation of data. Engagement led to a consensus across borders on the validity of the comparator. Sponsor was advised to extend study duration.



Treatment & prevention of a life-threatening condition with no approved therapies

Sponsor was planning a prospective single arm study from US and planned historical control arm. Acceptance of the overall study design and approach was questionable. Study design was adapted. The health economic plan was perceived as well designed and appropriate.