A Qualitative Comparison of German and United Kingdom Health Technology Assessments: Vedolizumab Case Study
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BACKGROUND

- Each national health technology assessment (HTA) authority has different requirements that need to be followed.
- A comparison of the HTA submissions and results for two countries for the same drug and indications can show the effect of these requirements on the final reimbursement decision for each country.
- Vedolizumab (Entyvio):
  - A monoclonal antibody for the treatment of ulcerative colitis and Crohn's disease; both are types of inflammatory bowel disease
  - Binds to a specific integrin, which results in gut-selective anti-inflammatory activity
  - Effectiveness measured by proportion of patients whose symptoms improved after a 6-week treatment
  - Effectiveness and tolerability shown in three phase 3 clinical trials: GEMINI I, II, and III
- The vedolizumab assessment was performed by the German Institute for Quality and Equity in Healthcare (IQWiG) for both indications simultaneously (A18–23), whereas the National Institute for Health and Care Excellence (NICE) did the assessment for the two indications separately (TA342 and TA352).

OBJECTIVES

- To compare and contrast the requirements of two national HTA authorities (Germany and the UK).
- To examine these differences in a comparison of the German HTA submission for vedolizumab in the indications of Crohn's disease and ulcerative colitis to the UK submission for the same drug and indications.

METHODS

- The submission and review processes of both countries' HTA authorities were reviewed from publicly available documents.
- The assessment of IQWiG and the decision of the Federal Joint Committee (BGA) for vedolizumab in the indications Crohn's disease and ulcerative colitis were compared with the NICE assessments, which took into account the opinion of the Evidence Review Group (ERG).

RESULTS

HTA Requirements and Procedures

- Germany:
  - Since 2011, manufacturers have been required to submit an Act on the Reform of the Market for Medical Products dossier (single or multiple indications) to the G-BA on the day of market launch.
  - The G-BA required to IQWiG (exception: orphan drugs)
- IQWiG considers evidence and makes recommendations to the G-BA for the extent of additional clinical benefit over the comparator defined.
- After written statements are received, the G-BA decides whether additional clinical benefit over the comparator is proven and the extent of additional benefit, which is the basis for the following price negotiation.
- If no additional clinical benefit is found, the price will not exceed that of the comparator.

- United Kingdom:
  - The drug is submitted for a single technology appraisal or multiple technology appraisal (multiple drugs with the same indication). A decision on which process will be used is made during the topic selection process by the Advisory Committee for Topic Selection.
  - NICE works with the Department of Health to draw up the scope of the appraisal. NICE invites consultants and a commentator organisation to take part in the appraisal.
  - A decision on whether the National Health Service (NHS) will fund the drug is based on cost-utility assessment compared to the NICE incremental cost-effectiveness ratio (ICER) threshold (usually £20,000-£30,000/QALY for England).
  - NICE experts draw evidence from multiple sources, such as the manufacturer, the ERG, and consultant specialists, and clinical and patient experts.
- The appraisal committee considers evidence, makes a recommendation, and submits to NICE either:
  - An appraisal consultation document (ACD). Usually NICE invites consultants, commentators, and the public; consultees help clarify issues, which leads to submission of the final appraisal document (FAD).

Table 1. Similarities Between the Two HTA Bodies' Review Processes

<table>
<thead>
<tr>
<th>Similarity</th>
<th>Germany</th>
<th>UK</th>
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<tbody>
<tr>
<td>Dossier sent to HTA authority</td>
<td>Yes, to the G-BA</td>
<td>Yes, to NICE</td>
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<tr>
<td>Review by independent organisation</td>
<td>Yes, by IQWiG</td>
<td>Yes, by the ERG</td>
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<td>Written statements publicly available</td>
<td>Yes</td>
<td>Yes</td>
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Table 2. Differences Between the Two HTA Bodies’ Review Processes

<table>
<thead>
<tr>
<th>Difference</th>
<th>Germany</th>
<th>UK</th>
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</thead>
<tbody>
<tr>
<td>For a new indication: at least 4 weeks after European Medicine Agency approval</td>
<td>All drugs approved for the indication</td>
<td>Upon invitation</td>
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<tr>
<td>Comparator</td>
<td>Appropriate comparative therapy (recommended by G-BA)</td>
<td>IQWiG: regular members of staff; clinical expert not involved in development process, advice only; G-BA: review by patient representative who does not have voting rights in decision</td>
</tr>
<tr>
<td>Review team</td>
<td>IQWiG: regular members of staff; clinical expert not involved in development process, advice only; G-BA: review by patient representative who does not have voting rights in decision</td>
<td>G-BA: review by patient representative who does not have voting rights in decision</td>
</tr>
<tr>
<td>Outcome</td>
<td>Clinical efficacy related to appropriate comparative therapy</td>
<td>Clinical efficacy and cost-effectiveness</td>
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<td></td>
<td>SHF (part of the G-BA) involved in all steps of the process: determination of appropriate clinical therapy, assessment, and price negotiation</td>
<td>Clinical efficacy against all drugs approved in the indication</td>
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Table 3. Reimbursement in Germany and the UK

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<th>Reimbursement</th>
<th>Germany</th>
<th>UK</th>
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<tr>
<td>Company sets initial price at launch</td>
<td>Price negotiation independent of submission process and often includes a PAS</td>
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<tr>
<td>Extent of additional clinical benefit is basis for price negotiation</td>
<td>Discount must apply to all current and future indications</td>
<td></td>
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<tr>
<td>If no additional clinical benefit is established, the reimbursed price will not be higher than that of the comparator</td>
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<td></td>
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<tr>
<td>Renegotiation in case of new indication</td>
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<td></td>
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Table 4. General Conclusions

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<tr>
<th>Conclusion</th>
<th>Germany</th>
<th>UK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early benefit assessment</td>
<td>Assessment of clinical efficacy and cost effectiveness</td>
<td></td>
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<tr>
<td>Manufacturer sets price at launch and negotiates rebate based on extent of additional clinical benefit</td>
<td>Price negotiation independent of submission process and often includes a PAS</td>
<td></td>
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<tr>
<td>Clinical efficacy against appropriate clinical therapy only with high demands on an NMA</td>
<td>Clinical efficacy against all drugs approved in the indication</td>
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CONCLUSIONS

- HTA evaluation processes in the UK and Germany differ and reflect the structure of the countries’ respective national health care systems (Table 4).
- Each system has its strengths and weaknesses. Due to the differences in the HTA evaluation process, different strategies are necessary in each country to achieve successful market access for new drugs and/or indications.

REFERENCES


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