HTA expert Interview Guide:

Acceptability of a complex treatment-sequencing model for relapsing-remitting multiple sclerosis from an HTA perspective

Date of interview: _____/_____/_____
MM DD YYYY

Interview start time: _____

Interview end time: _____

Name of interviewer: _____, _____
Last First

Section 1: Introduction (5 minutes)

The purpose of today's interview is to assess the acceptability and desirability of a cost-effectiveness model that can include a sequence of relapsing-remitting multiple sclerosis (RRMS) treatments from a health-technology assessment (HTA) body perspective.

Today's interview agenda will take approximately 80 minutes. During that time, questions will be asked about the following topics:

- *The desirability of treatment-sequencing models in general and in RRMS*
- *The acceptability of complex health-economic models*
- *Acceptable ways to handle variability, heterogeneity and uncertainty in natural history*
- *The acceptability of the inclusion of the physician perspective*
- *The desirability of the inclusion of the patient perspective*

Do you have any questions?

Before we begin the interview, do I have your permission to audio-record this interview? ☐ *Yes* ☐ *No*

Section 2: Background and expertise (5 minutes)

1. What is your professional background and experience with health technology assessments?
    a. PROBE: Which organization?
    b. PROBE: Specialty?
    c. PROBE: Years of working experience for your HTA body?
    d. PROBE: Disease areas

Section 3: Desirability of evaluating RRMS treatments as part of a sequence (15 minutes)

Treatment discontinuation and consequent treatment switching, for reasons of safety or efficacy, is a common issue in many disease areas (oncology, rheumatoid arthritis, multiple sclerosis).

1. Do you have experience with health economic or disease models that model multiple lines of treatment?
    a. [If experience]
        i. In what indication(s)?
        ii. In Rheumatoid arthritis?
2. How are the consequences of treatment discontinuation usually captured in the assessments you perform?
    a. PROBE: Switching captured?
    b. PROBE: In what types of analyses or assessments?
    c. PROBE: Do you think these consequences are sufficiently captured?

3. To what extent do you consider treatments as part of a sequence in your assessments?
    a. PROBE: In *what indications* or situations?
        i. What if you assess a treatment indicated for one treatment line?
    b. PROBE: How do you usually take treatment sequences into account?
        i. Using a (health-economic) model?
        ii. In some other systematic way?
    c. PROBE: *How common* is it to take sequences into account?
        i. [If appropriate given answers 3.b.i. and ii] Why are treatment-sequencing models more common in some diseases than in other diseases?
        ii. In what disease or situations is it a problem if sequences aren't captured?
    d. PROBE: Could you think of any r*easons why or why not* these are (commonly) taken into account?
        i. [If not]: Quality?
        ii. [If not]: Complexity?
        iii. [If not]: Relevance to the research question or decision problem?
4. Where do you see opportunities for a treatment-sequencing model in RRMS to inform HTA decision making?
    a. PROBE: Could it be useful to assess individual products in a sequence?
    b. PROBE: Could it be useful to assess treatment sequences in their entirety?
    c. PROBE: What outcomes would you assess?
        i. Effectiveness?
        ii. Cost-effectiveness?
        iii. Budget impact?

Section 4: Acceptability of complex models (15 minutes)

1. Do you have experience with complex health economic models, like patient-level simulations or discrete event simulations?
    a. PROBE: what type of model(s)?
    b. PROBE: in what indication(s)?

2. How does your HTA body regard more complex health economic models?
    a. PROBE: Does it usually accept complex models?
    b. PROBE: What are reasons to accept such models?
    c. PROBE: What are reasons to not accept such models?
    d. PROBE: What are minimal requirements to accept such models?

More complex models usually require more data than standard Markov or three-state partitioned survival models.

3. What are your agency's requirements regarding the data in more complex models?
    a. PROBE: Amount of data (gaps)?
    b. PROBE: Quality?
    c. PROBE: Source?
        - What sources?
            - DCE?
            - Expert opinion?
            - RWE? -> examples

4. How are these requirements different in complex models than in standard models?

5. Could you give examples of pragmatic approaches to handle data gaps in complex models that were still acceptable for the purpose of the assessment?
    a. PROBE: Have you ever observed a willingness for your HTA body to provide data in a confidential manner to inform an assessment or modelling question?

6. What are requirements regarding the handling of uncertainty in the assessment of a complex model?
    a. PROBE: How are requirements different compared to "standard" less complex models?

Models are usually submitted in MS Excel, but this software is not the most suitable for complex models.

7. To what extend does your HTA body accept models that are programmed in programming languages that allow for more complex simulations?
    a. PROBE: Has R been accepted?
    b. PROBE: Others than R and Excel?

Section 5: Acceptable ways to handle variability, heterogeneity and uncertainty
(15 minutes)

1. What is your experience with health economic assessments in RRMS?
    a. PROBE: What RRMS drugs have you reviewed?
    b. PROBE: In what year did you perform the assessment in RRMS?
    c. PROBE: Are you familiar with RRMS models?
        i. [If yes]: what are the strengths and weaknesses of the existing models?

2. How important is it for your HTA agency to capture the variability and/or heterogeneity in disease trajectories that patients can experience?
    a. PROBE: How should variability and/or heterogeneity be captured?
        i. By subgroups?
        ii. Distributions around disease characteristics?

3. What is the relevance of subgroup assessments for RRMS for appraisals conducted by your organization?
    a. PROBE: What are the criteria for determining the relevance of subgroups?
    b. PROBE: What are relevant subgroups in RRMS specifically?

Treatment-sequencing models model a number of treatments in a sequence. For most treatments, the efficacy in 1st line can be obtained from randomized controlled trials. However, few treatments are investigated in 2nd or 3rd line, and if they are, no evidence is available by prior treatment.

4. What is an acceptable way for your HTA agency to address the lack of efficacy data in later -line and by prior treatment?
    a. PROBE: Expert opinion?
    b. PROBE: Real-world evidence?
    c. PROBE: Scenario analyses?

Section 6: Acceptability of including physician perspective (15 minutes)

A treatment-sequencing model might incorporate the physician perspective in the decisions regarding when to switch treatment and what treatment should be next.

1. What is your experience with models that have incorporated the physician perspective?
2. What is your opinion about models that have incorporated the physician perspective?
3. What is your opinion on the incorporation of the physician's perspective as described?
    a. PROBE: are decision rules as used in clinical practice of any value to HTA bodies?
4. What would be your requirements regarding the derivation of clinical decision rules for switching if such rules would be incorporated in the model?
    a. PROBE: How many physicians should deliver input?
    b. PROBE: Country-specific decision rule?
    c. PROBE: Method to elicit physician's preferences?
    d. PROBE: Validation?

Section 7: Desirability of including patient perspective (10 minutes)

- *Patients have a voice in decisions regarding their treatment, for example by refusing higher-risk treatment options.*
- *A treatment-sequencing model may not only incorporate the physician perspective in the decision rule to switch to alternative treatments, but also incorporate the patient perspective.*

1. Do you have experience with models that have incorporated the patient perspective in some way?
    a. PROBE: examples? -> Reference?
    b. PROBE: what indications?

2. Would it be of added value to incorporate the patient perspective into the model by assuming that the patient can influence the physician's decision?
    e. PROBE: incorporate patient's risk tolerance?

3. What would be your requirements regarding the derivation of patient preferences if such preferences would be incorporated in the model, for example as part of a decision rule?
    a. PROBE: How many patients should deliver input?
    b. PROBE: Country-specific decision rule?
    c. PROBE: Method of elicitation?
    d. PROBE: Validation?

Closure

Those were all the questions. Is there anything else that in your view would be important for us to know?

-- **END OF RECORDED INTERVIEW –**
