ISPOR 2021 Issue Panel: Defining Established Clinical Management in the Era of Managed Access In HTA

Tuesday 30th November 12:30–1:30pm

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Introduction

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The Issue: Setting the Scene

Different health technology assessment (HTA) systems across Europe have different reference cases with respect to which treatments should be considered comparators in economic evaluations

This is further complicated by treatments that are available only through managed access agreements (MAAs)

- Treatments available through MAAs do not typically represent "standard of care" and bring with them additional uncertainty e.g. longer-term reimbursement status, clinical benefit, and/or the price of the drug
- MAAs are increasingly being used as a route to market access,[1] meaning that in some disease areas, standard clinical practice is dominated by treatments made available through such arrangements

5/11 drugs in multiple myeloma appraised by NICE since 2018 have been funded through the CDF

In France, Germany, Italy, Spain and England, all currently available CAR-T therapies are available through outcome-based MAAs[2]

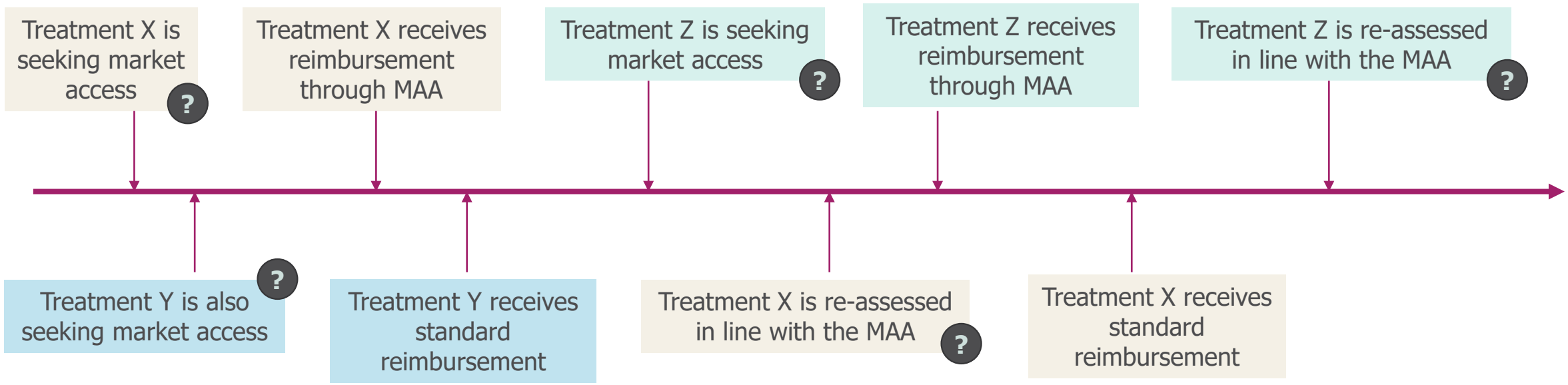
Since 2019, NICE has separately appraised 3 treatments for SMA, two of which are available through MAAs requiring additional evidence generation (one in development)

The use of MAAs to gain market access is expected to increase as treatments become more expensive and/or associated with more clinical uncertainty, meaning it is important to consider the appropriateness of current HTA processes for defining comparators in this context

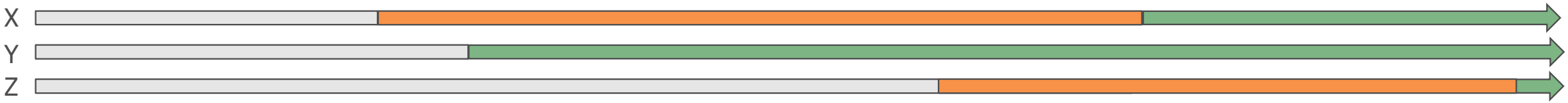
1. Kanavos, P., Ferrario, A., Tafuri, G. & Siviero, P. (2017) Managing Risk and Uncertainty in Health Technology Introduction: The Role of Managed Entry Agreement. *Global Policy* 8(2), pp. 84-92.
2. Hatikou, M., Michaeilidou, F., Theodorou, P. (2020) PPM8 The Reimbursement Schemes of CAR-T Therapies Followed in France, Germany, Italy, Spain, UK and the Proposed Scheme for Greece. *Value in Health*, 23, p. S688.

Abbreviations: CDF, Cancer Drugs Fund; EMA, European Medicines Agency; HTA, health technology assessment; MAA, managed access agreements; NICE, National Institute for Health and Care Excellence; SMA, spinal muscular atrophy.

The Issue: What Are Your Comparators?



Reimbursement Status



What do we want to understand from today's issue panel?

- What is the rationale for different approaches to defining comparators across Europe in HTA?
- Do these discrepancies matter?
- Do we need to make any changes to the approach of assessing therapies considering increasing MAAs?

Abbreviations: HTA, health technology assessment; MAA, managed access agreements.

The Panel

Exclusive

Jacoline Bouvy

Technical Director for NICE Scientific Advice

Inclusive

Gérard De Pouvourville

Professor of Economics; ESSEC Business School

Academic

Mark Sculpher

Director, Centre for Health Economics University of York

Abbreviations: ESSEC, École Supérieure des Sciences Economiques et Commerciales; NICE, National Institute for Health and Care Excellence.

Selecting your NICE comparator

ISPOR Europe issue panel, 30 November 2021

‘Defining established clinical management in the era of managed access in HTA’

Dr Jacoline Bouvy

Technical Director, NICE Scientific Advice

NICE National Institute for Health and Care Excellence

Relevant comparator(s) are identified at scoping stage

Scoping determines the nature and content of the evidence to be included in the assessment phase of the appraisal

Final decision on relevant comparators sits with Committee

NICE

What does the NICE methods guide (2013) say about selecting the right comparator?

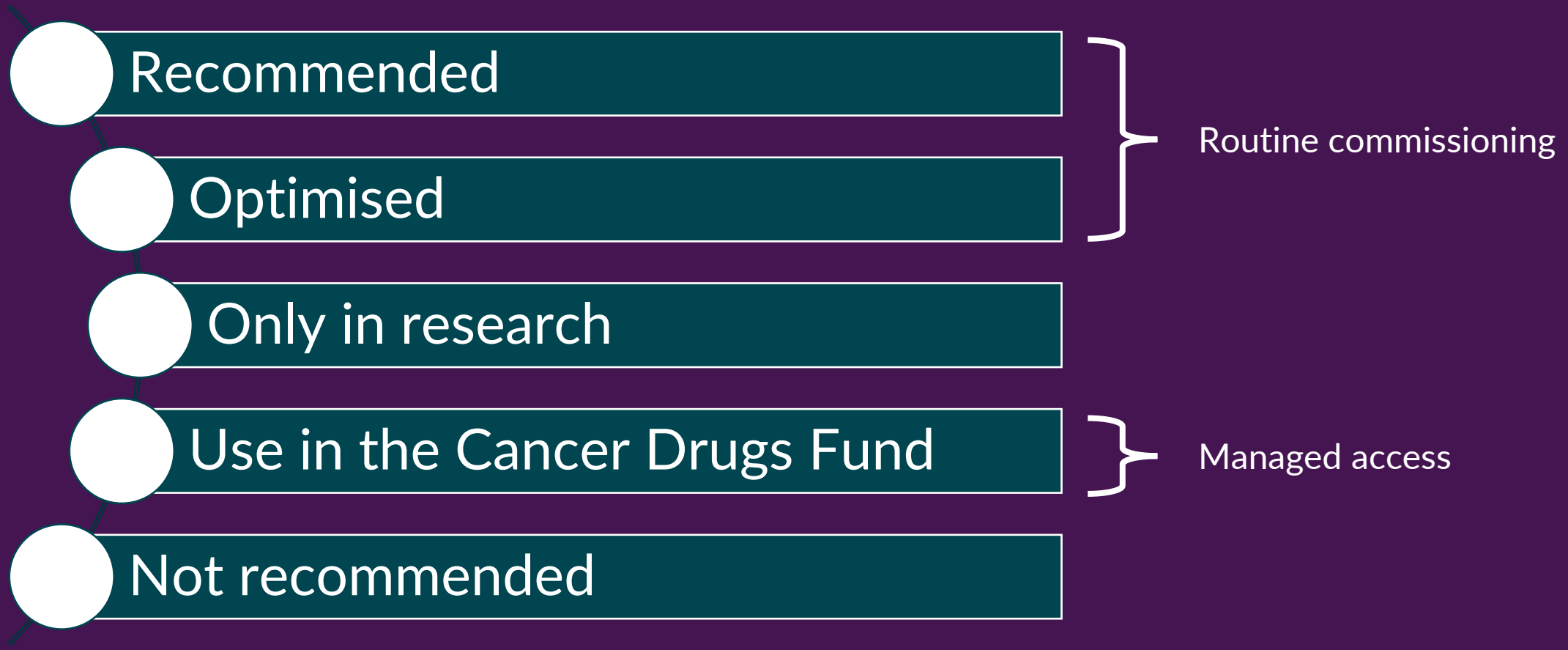
'When selecting the most appropriate comparator(s), the Committee will consider:

- Established NHS practice in England
- The natural history of the condition without suitable treatment
- Existing NICE guidance
- Cost effectiveness
- The licensing status of the comparator'

(*section 6.2.1*)

NICE

What recommendations can the appraisal committee make?



NICE

All these criteria need to be met for a CDF recommend-dation:

NICE

Drug cannot be recommended due to clinical uncertainty

Drug has plausible potential to be cost effective at the current price

Data collection could reduce uncertainty

Ongoing studies will provide useful data and CDF data collection is feasible

Managed access is not routine commissioning

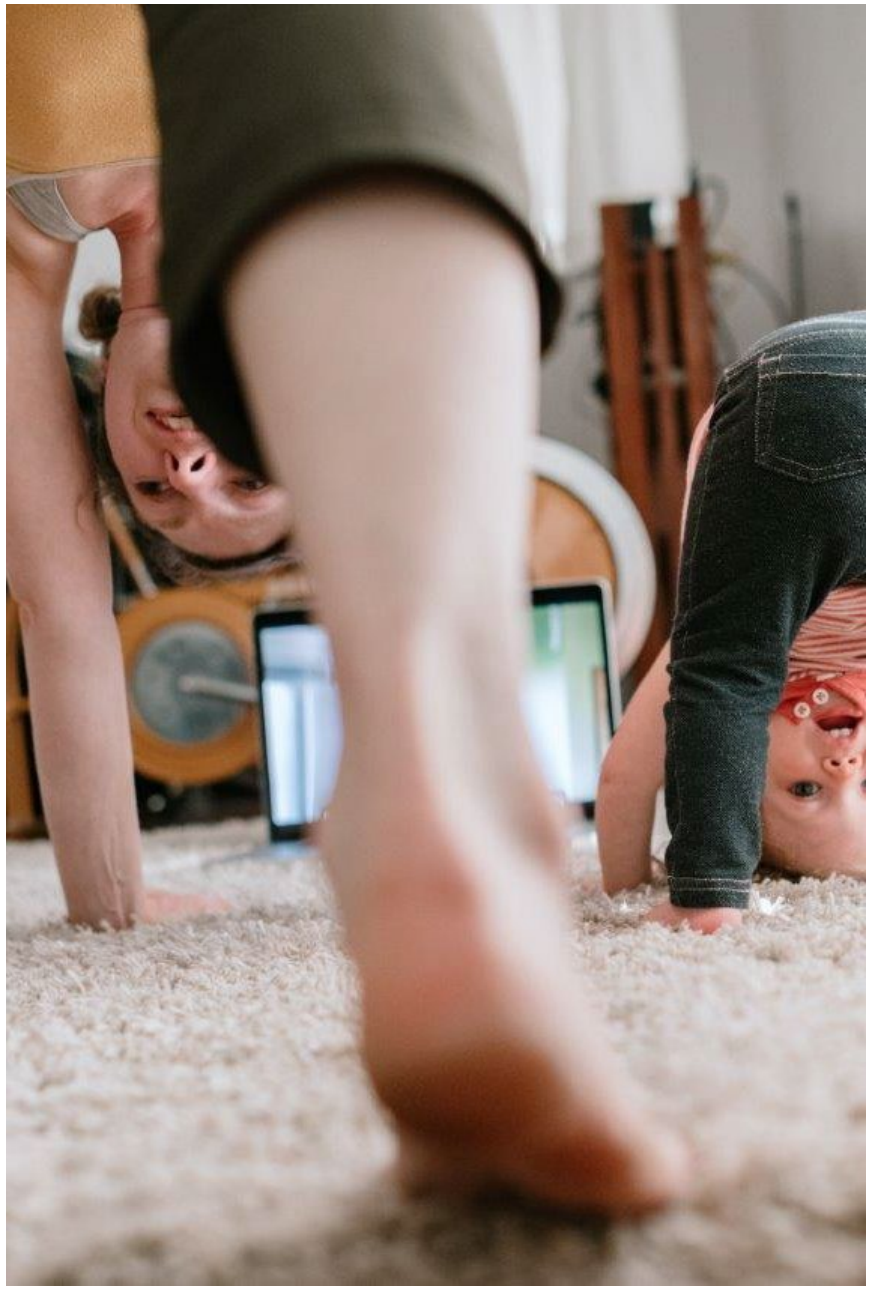
- When uncertainty is too great to make a recommendation, due to clinical uncertainty, the drug cannot be considered established clinical practice
- Subsequent funding of CDF drugs once they exit is not guaranteed as NICE might not recommend the drug for routine commissioning at end of the managed access period

(*source: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisal-guidance/cancer-drugs-fund/CDF-comparator-position-statement.pdf*)

NICE

What about the future?

NICE



Methods and process review, draft CHTE manual for consultation (October 2021):

‘Technologies that NICE has recommended for use in managed access are not considered standard care and are not considered suitable comparators’

Innovative Medicines Fund (IMF)

Proposed £340m fund to enable managed access for non-cancer drugs

NICE National Institute for Health and Care Excellence

Thank you.

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A brief reminder:

- French HTA Agency: the HAS (Haute Autorité de Santé)
- Market access for drugs:
  - A clinical and public health assessement performed by the Transparency Commission:
    - Clinical Benefit (SMR): leads to reimbursement
    - Clinical Added Value: relative value vs existing alternatives and to pricing
  - For drugs which companies claim a moderate to high clinical added value, the Commission for the Economic and Public health Evaluation (CEESP) will assess a cost-effectiveness dossier provided by companies (roughly 10% of new applications)
  - Dossiers follow a parallel track

Relevant comparators for the CT *

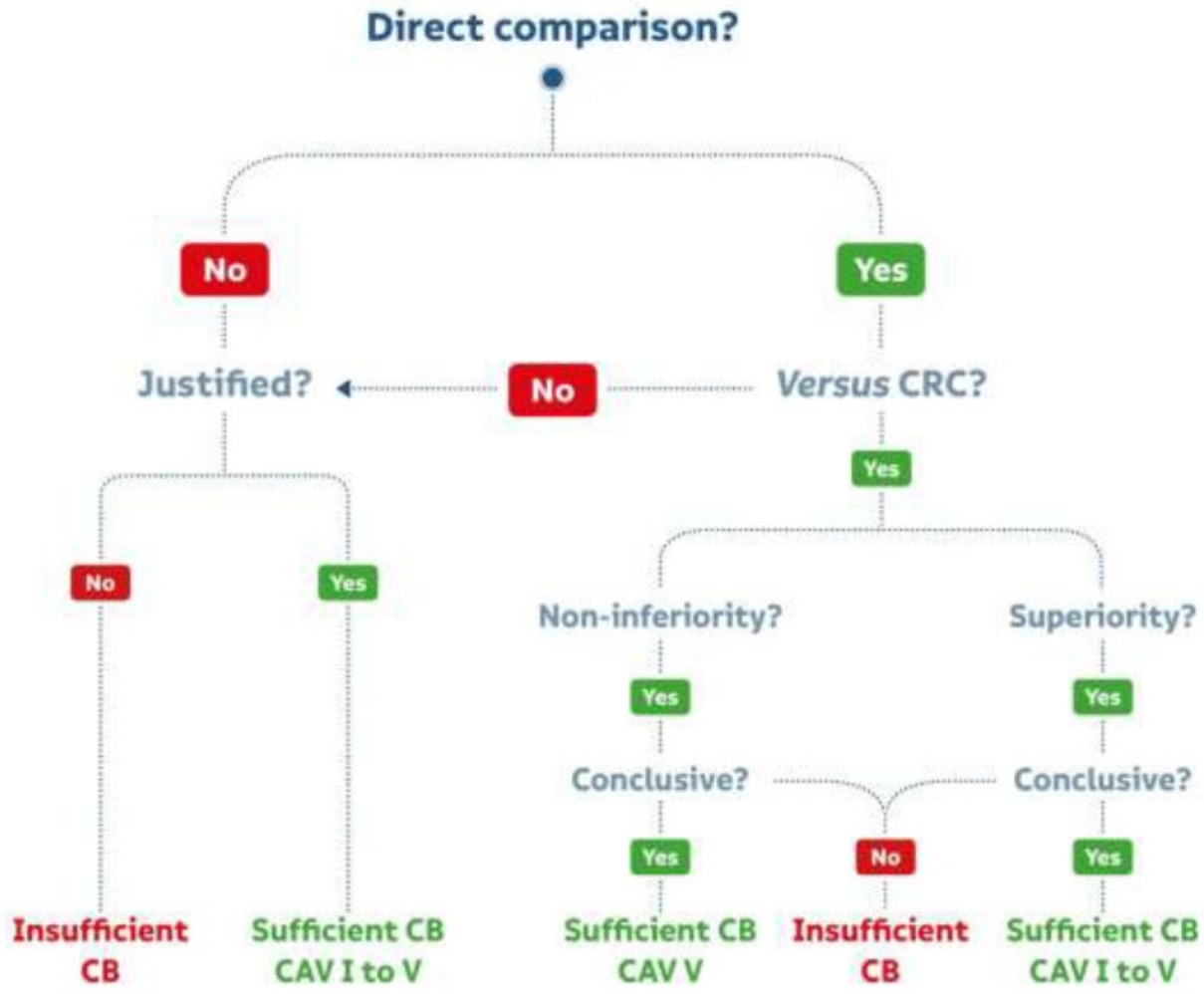
- Broad definition:

> A clinically "relevant" comparator may be a medicine (active substance or placebo, with or without MA), a medical device, a procedure or any other non-medicinal therapy (or diagnostic method). It can be use at the same step of the care pathway as the new medicine and aims the same patients.

- Application:
  - A direct comparison with a clinically relevant comparator, in a double-blind, randomised trial, is expected wherever possible.
  - Indirect comparisons are acceptable if performed according to pre-defined guidelines
  - Real world data may be acceptable for some cases

CT decision tree

Figure 1. Comparison in the Transparency Committee's assessment



In practice:

- The CT identifies and selects what it considers as a relevant comparator ;
  - Clinical relevance
  - Used in the French context….
  - According to HAS and medical societies guidelines

- If the RCT does not include the selected comparator, this has a potential to reduce the assessed Clinical Added Value, on the basis of uncertainty: data missing for a complete assessment

Cost-effectiveness and CEESP

- The ICER has no impact on coverage
- There is no threshold
- The impact on price is modest

Outcomes

- Main criterion: compliance to the guide
- Accepted with no or minor restriction
- Accepted with important restrictions
- Rejected because of major restrictions:
  - Major deviation from the guide
  - Acceptable methodology, but high uncertainty

Cost-effectiveness and the CEESP

Guideline 5

The reference case analysis should identify all clinically relevant interventions in the population analysed.

The arguments supporting the inclusion or exclusion of an intervention in the reference case analysis should be clearly set out.

The interpretation of the results of the evaluation should consider the degree of exhaustiveness of the comparators used. Given that all comparators need to be taken into account to evaluate cost-effectiveness, the risk of excluding an intervention likely to be on the cost-effectiveness frontier, and its consequences, should be discussed.

Implications

- All relevant interventions should be identified (including non-drug);
- If an intervention is excluded, the exclusion should be justified and its impact on the ICER estimated;
- What interventions?
  - Existing published data and published prices or maximum compensation amounts
  - Drugs under EMA scrutiny may be included if they are incuded in a Temprorary Utilisation Program (ATU), or under early filing with HAS
  - Low usage is not a reason for exclusion
  - Off-label utilisation of a drug can be considered if it is current practice

The key message:

- The efficiency frontier has to be as exhaustive as possible;
- If not, major restriction
- Some discretionary power in the assessment of the completeness of the list of comparators….
  - Clinical expertise has little impact

Consideration 1: MAAs and routine access

- MEAs come in many forms
- Some may not provide access to all relevant patients
- Example: research based MAAs

→ Not routinely available = not relevant comparator

Consideration 2: Frequency of updates

- How often is guidance reviewed and updated?
- More frequent updates allow quicker responses to completion of MAAs

→ Not relevant comparator when in MAA

- Less frequent updates, implications of completed MAAs for decisions unclear

→ Relevant comparator when in MAA

Consideration 3: new assessment after an MAA

- Is there a full re-evaluation of product after a MAA?
- If so, it becomes the intervention of interest
- Any other products evaluated during the MAA become comparators

→Not relevant comparator when in MAA

- No full re-evaluation at completion of MAA means comparison with other new products may not be undertaken, with no guidance to decision makers

→Relevant comparator when in MAA

Methods if MAA product a relevant comparator

What price?	• Future price changes always uncertain • Guidance conditional on price
Uncertain evidence	• Evidential uncertainty inescapable • Without frequent updates, best evidence available
No routine use after MAA	• Updating guidance more straightforward

Conclusions

- Discrepancies across Europe may be explained by some considerations
- Discrepancies matter less than failure to offer timely guidance
- Appropriate more important than consistent
- Depends on frequency of updates and use of re-evaluations after MAAs

Thank you!

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