

Annex 7: health technology assessment process.

1 Purpose

- 1.1 The evaluation framework will guide the evaluation of two antimicrobials selected through the procurement process to develop and test innovative models for the evaluation and purchase of antimicrobials.

2 Key stages in the evaluation

- 2.1 The main stages in the evaluation of each of the antimicrobials are:
- a. Completion of a scoping document by NICE and the DHSC Policy Research Unit in Economic Methods of Evaluation in Health and Care Interventions (EEPRU).
 - b. Submission of relevant evidence and information by the company. Some of this information may be provided during the procurement process, but a full submission will be required following the scoping phase.
 - c. Completion of a protocol for the evaluation work by EEPRU.
 - d. Completion of a HTA report by EEPRU, including a step to allow the company to review a draft for factual accuracy.
 - e. NICE committee process that reviews the HTA report and considers the added value from use of the product and most plausible assumptions on the clinical and economic assessment of value.
 - f. Completion of a NICE guidance document based on the HTA report and Committee considerations. The guidance will include preliminary recommendations on the value of the selected antimicrobial to the NHS, to inform subsequent negotiation between the companies and NHS England & NHS Improvement.
 - g. Completion of final NICE guidance to reflect the outcomes of the commercial negotiation.

3 Process considerations

- 3.1 The timeline for steps (a) to (f) is anticipated to be 12 months. Step (g) will be undertaken later following the commercial negotiation. The evaluation of the two antimicrobials will be undertaken in parallel, such that the commercial negotiations can commence for both products within the 12 months' timeline.
- 3.2 In this project, the product evaluations will be undertaken by the EEPRU supported by other experts and DHSC policy research units as appropriate.
- 3.3 A special committee will be convened at NICE for this project. It is envisaged that this will comprise approximately 10 members from current NICE committees with an additional 6 members with specialist expertise (e.g. treating clinicians, transition modelling experts and

clinical data specialists). Members will be appointed by the Project Team with oversight from the Project Board. The appointment for the committee chair has been made (Professor Amanda Adler), so that she will be able to contribute to the scoping process.

- 3.4 Part of the objective of the current project is to develop arrangements for the evaluation and purchase of new antimicrobials that could potentially be rolled out more widely, depending on the eventual policy informed by this project. It is therefore important that the resources applied to antimicrobial evaluation are not unrealistic and that a similar approach could be scaled up as necessary to a broader range of products. As a guide, resources equivalent to those employed by Assessment Groups working on a NICE multiple technology appraisal (MTA), are considered a realistic starting point for the evaluation of each of the antimicrobials. It may be reasonable, however, to apply some resources in excess of this level to reflect that these are the first evaluations and that some future efficiencies are likely should the approach be rolled out more widely.
- 3.5 The process will require a company submission of relevant evidence, but this does not need to include an economic model. However, where available, company health economic models will be taken into account.
- 3.6 The NICE guidance documents produced in this project will not be Technology Appraisals guidance and some of the process elements included in the Technology Appraisal process, such as consultation on the preliminary recommendations and final guidance, will not be included.
- 3.7 To the extent possible, outputs from the evaluation of the selected products will be made publicly available. Arrangements for handling commercial in confidence and academic in confidence information will be based on NICE's current processes.

4 Methods considerations

- 4.1 The methodological learning captured in the [EEPRU report Framework for Value Assessment of New Antimicrobials](#) may guide much of the work. In addition, where applicable, principles in the [NICE guide to the methods of technology appraisal](#) may be followed. Other methods and models for evaluating antimicrobials may also be considered and adopted as appropriate. However, given that these evaluations are highly complex, EEPRU colleagues will be expected to apply their expertise and judgement without being constrained by a prescriptive methodological framework.

- 4.2 EEPRU colleagues may seek specialist support for elements of the evaluations as appropriate. Provision has been made for input from other DHSC research units; Operational Research for Emergency Response and Strategic Planning Analysis (OPERA), and Health Protection and Improvement with Operational Research (HAPIOR). Further specialist input may be required.
- 4.3 The scoping of the evaluations is a critical and complex phase. The scoping phase will be co-managed by EEPRU and NICE. The final scope will be signed off by NICE. To be useful in the subsequent commercial negotiations, the HTA reports will endeavour to cover the full scope of the Marketing Authorisation (MA). Depending on the product, the MA could potentially include multiple scenarios across different pathogens and clinical syndromes. Based on the resource constraints and timelines, it may not be feasible to comprehensively consider and develop health economic models for all of these scenarios.
- 4.4 It is envisaged that through scoping and protocol development, the following will be identified and agreed:
- a. One or more pathogen/clinical syndrome combination for detailed study and health economic modelling. This should be carefully considered, and be where the product has the greatest potential for addressing unmet clinical need or beneficially impacting public health.
 - b. Other important pathogen/clinical syndrome combinations that need to be considered within the HTA report but where bespoke economic models will not be developed. In these cases, a summary of relevant available quantitative and qualitative information will be provided.
- 4.5 It is important that, in addition to the clinical value that is normally considered in HTA, other elements of value that new antimicrobials generate may be considered, including, but not limited to:
- a. Diversity value (having a range of treatment options available)
 - b. Transmission value (avoiding onwards spread of pathogens in the population)
 - c. Enablement value (enabling other treatments and procedures to take place, e.g. chemotherapy, organ transplant, surgical procedures)
 - d. Spectrum value (benefits of replacing broad spectrum antimicrobials with narrow spectrum antimicrobials).
 - e. Insurance value (having antimicrobials available for sudden increase of infections with pathogens resistant to existing antimicrobials).
- 4.6 In principle, these elements of value can be captured in terms of quality-adjusted life years (QALYs). A number of key parameter inputs for any type of model are unlikely to be available from the literature and may need to be estimated through expert elicitation.

Depending on timelines and resource availability, a formal expert elicitation exercise may be considered as a method for more robustly quantifying expert opinion. For the pathogen/clinical syndrome combination(s) selected for detailed evaluation, value should be captured in QALYs where possible. Further considerations include:

- a. The analysis needs to include an estimate of benefits at the population level as well as for the patients treated
- b. Several stewardship strategies might need to be modelled and compared (e.g. rotation of antimicrobials, mixing protocols, combination strategies) to identify the optimal usage scenario
- c. Forecasting models and/or more complex dynamic transmission models may be needed to synthesise the available evidence
- d. Microbiological response rates, as well as clinical cure rates and other individual patient outcomes, may need to be included in order to accurately reflect plausible rates of transmission and resistance, as patients who are cured clinically may still contribute to the spread of pathogens
- e. For some model parameters, reliable evidence might not be available and expert elicitation might be needed to inform some model assumptions

4.7 Given the high uncertainty in evaluating the benefits quantitatively, QALY estimates may need to be expressed as ranges rather than as central estimates. The analysis will, where possible, be explicit about what elements of value are included in the economic model and which elements are not, together with explanations of why some elements of value are not included.

4.8 For the elements of value not included in the economic model, summaries of the relevant available quantitative and qualitative information may be included as part of the evaluation.

4.9 Important evidence on the value of a new antimicrobial could potentially be derived from pre-clinical studies such as the in-vitro antimicrobial activity spectrum and pharmacokinetic and pharmacodynamic (PK/PD) profiles. Such evidence, where relevant, may be included in the product evaluations.

4.10 Given the anticipated high uncertainty at the time of the initial assessment, the key data for collection following the assessment will be identified.

5 NICE committee considerations

5.1 The committee stage is crucial in developing NICE guidance about the value of the antimicrobials and to inform subsequent commercial negotiations. It is important, however, that in the appointment of the committee members it is clear that the task differs from

normal NICE committee work. The differences between this project and NICE Technology Appraisals of new medicines are summarised in Appendix 1.

- 5.2 The committee will evaluate the evidence to identify the most plausible ranges of benefit of the antimicrobial under evaluation through:
- a. Review of quantitative estimates of benefits for the pathogen/clinical syndrome combination(s) selected for detailed evaluation, including consideration of potentially high uncertainty where the evidence supporting model inputs is limited (e.g. based on expert elicitation)
 - b. Review of relevant available quantitative and qualitative information for elements of value not included in the health economic modelling for the pathogen/clinical syndrome combination(s) selected for detailed evaluation
 - c. Review of relevant available quantitative and qualitative information for the pathogen/clinical syndrome combinations not selected for detailed evaluation
 - d. Contributing to guidance development based on the HTA report from EEPRU. The committee consideration will lead to NICE guidance documents with initial recommendations that inform subsequent commercial negotiations between the companies and NHS England. The committee considerations are likely to include ranges of value, expressed in QALYs where possible. The committee will not be expected to make binary yes/no decisions on whether the products should be recommended for use in the NHS.
 - e. Contributing to the development of final NICE guidance reflecting the outcomes of the commercial negotiation.

6 Future Policy

- 6.1 Future policy, including details of process and organisation roles, will be informed by the outcomes from this project and that no assumptions should be made about the future arrangements for the evaluation of antimicrobials.

APPENDIX 1: COMPARISON OF ANTIMICROBIAL EVALUATION IN THIS PROJECT AND NICE TECHNOLOGY APPRAISALS

	Project	NICE Technology Appraisals
Purpose of the NICE evaluation	To produce guidance on the value of the new antimicrobial with initial recommendations to inform commercial negotiations and final guidance that reflects the outcomes of the commercial negotiations.	To produce guidance on the use of the new medicine, funding of which is mandatory for commissioners in the NHS in England.
Procurement process	Bespoke arrangements (see separate document)	Referral by Secretary of State for Health and Social Care
Process	Bespoke process modelled on the NICE MTA process.	NICE technology appraisal processes.
Methods	Flexible methods at the discretion of EEPRU taking account of the NICE guide to the methods of technology appraisal.	NICE guide to the methods of technology appraisal.
NICE committee role	To review the EEPRU HTA report and consider the plausible range of value (quantitative and qualitative). To translate a range of potential value to the NHS into guidance.	To consider the assumptions and plausibility of value estimates and to translate this to guidance to the NHS.
Output from the NICE committee stage	Preliminary recommendations in draft guidance and final NICE guidance.	NICE Technology Appraisal guidance.
Expected impact of the evaluation on NHS use of the product	The guidance will inform commercial terms rather than a binary yes/no decision. The guidance will also inform NHS usage by identifying the preferred usage scenario.	Guidance pivotal to whether or not, and under what circumstances, the technology is used in the NHS.
Funding mandate	Does not apply	Applies