

UNIT-IV

Assessment of a new antibiotics



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Assessment of a New Antibiotic

- Antimicrobial Resistance (AMR) occurs when microbes (bacteria, viruses, fungi, and parasites) change in ways making the medications used for curing the infections ineffective. If new antibiotics are not introduced, the patients will die due to the previously treatable infections.
- However, a major issue is adequate evaluation of the antibiotics, particularly by payers and/or Health Technology Assessment (HTA) Bodies, to take account of AMR and reflect the full benefit provided to patients and society.

Two Key Challenges

- 1) Clinical trials are designed for establishing non-inferiority, while HTA bodies require demonstration of clinical superiority.
- 2) HTA bodies do not have a mechanism to evaluate the health benefits of antibiotics, and control the rise in AMR.

Elements of Value Relevant to Antibiotics: these are given in the table below 4.14 and explained as follows

Table 4.14: Additional Elements of Value Relevant to Antibiotics

Relevant Benefits included in Traditional HTA	Other Types of Benefit of Possible relevance to Antibiotics
Health gain	Insurance value
Unmet need	Diversity value
Cost offsets	Diagnostic value
Productivity benefits	Uniqueness or innovation value
	Enablement value
	Spectrum value

Relevant Benefits included in Traditional HTA: are

Health Gain

- 1) It includes life extension and quality of life gains.
- 2) It is accepted as a criterion for positive HTA recommendation.
- 3) Evidence required by HTA bodies is often inaccessible for antibiotics (superiority trials).

Unmet Need

- 1) It includes severity of disease and current availability of alternative treatments.
- 2) It involves use of priority pathogen lists.

Cost Offsets

- 1) It includes the reduction in costs in other areas as a result of use of new medicine.
- 2) It involves use of modelling studies and/or evidence from clinical trials.

Productivity Benefits

- 1) It involves profits or losses related to value of patient's time, receiving medical care or out of work.
- 2) It involves use of modelling studies and/or evidence from clinical trials/observational studies.

Other Types of Benefit of Possible relevance to Antibiotics: are

Insurance Value

- 1) It is the value of treatment available in case of catastrophic health events, e.g, outbreak of MDR infections which cannot be controlled by existing last-line antibiotics.
- 2) It is analogous to availability of a fire engine.
- 3) It also needs to add in the "precautionary principle".
- 4) It involves use of modelling studies.

Diversity Value

- 1) It is the selection pressure, i.e., the antibiotic is able to eliminate susceptible species of bacteria but no other resistant pathogens; thus these pathogens survive and multiply, making the antibiotic ineffective.
- 2) It involves evidence that reducing selection pressure by withdrawing antibiotic for a period of time may result in restoration of susceptibilities.
- 3) It involves use of modelling studies.

Diagnostic Value

- 1) If infection is diagnosed at an early stage, appropriate antibiotic therapy can be started earlier.
- 2) It needs evidence of test accuracy.

Uniqueness or Innovation Value

- 1) It is the potential value associated with new or unique mechanism of action.
- 2) Antibiotics with novel mechanism of action may avoid problems of cross-resistance occurring in many existing classes.
- 3) Discovery of new mechanism of action of an antibiotic makes it easier for 'follow on' products to enter market.
- 4) It needs evidence of new mechanism of action.

Enablement Value

- 1) It is the availability of effective antibiotics supporting many surgical procedures and treatments for people having compromised immune systems.
- 2) It involves use of modelling studies.

Spectrum Value

- 1) Narrow spectrum antibiotics may be more valuable than broad spectrum ones as the former can reduce spread of AMR by preventing 'collateral damage' to the microbiome.
- 2) It depends on the antibiotic.

Reasons for which additional elements of value for antibiotics are required:

- Given below are the reasons for which additional elements of value for antibiotics are required:
- 1) AMR is a Public Health Priority: The rise of AMR is a serious threat, control of which is a priority for the national and international health organizations. The current HTA methods do not account for the value of reducing this public health threat, e.g., of the insurance value of having a treatment available in case of a future major or rapidly intensifying resistance problem.
- 2) Diverse Set of Non-Inferior Antibiotics is Valuable to Society: Since AMR is increasing widely, it has become valuable developing a new antibiotic for MDR pathogens, even if it is ineffective than the existing antibiotics in treating susceptible (non-resistant) pathogens. This concept is unique to antibiotics and is not considered by HTA bodies.

- 3) Non-Clinical and Microbiology Data are important for Demonstrating the Value of Antibiotics: Non-clinical and microbiology data for antibiotics can predict their results. Due to the difficulties in conducting clinical trials for antibiotics for MDR pathogens, regulators accept these alternative types of evidence as part of the approval process in areas of high unmet need.
- 4) Antibiotics have Benefits that go Beyond the Patient Treated: When one patient is treated with an antibiotic, the spread of the infectious disease is reduced thus benefitting the population.
- 5) Antibiotics Enable Other Types of Treatment and Procedures: Apart from treating infections, antibiotics also reduce the risk associated with other types of treatment such as surgery and chemotherapy.