

Baltic Guideline for Economic Evaluation of Pharmaceuticals (Pharmacoeconomic Analysis)

Economic evaluation of pharmaceuticals is the application of analytical methods to define cost and consequences of drug treatment or other interventions to support decision-making in resource allocation in health care.

1. Objective of the guideline and target audience

There is a growing need to consider cost and cost-effectiveness of treatments as a part of health care decision making in all countries. There are several scientific and regulatory guidelines available, however, they cannot be generalised to every country, as the health care systems and financing principles differ. The Baltic states (Latvia, Lithuania and Estonia) share similar social and economic conditions. All three countries have decided to use pharmacoeconomic analysis as a basis for drug reimbursement and other state funding decisions.

The present guideline provides basis for the pharmacoeconomic application submitted as a part of application to include new drug in the positive list for reimbursement or other state funding and is aimed for use by the Baltic state institutions performing pharmacoeconomic assessment of a new drug as a basis for reimbursement and setting a reasonable price of a drug for reimbursement.

The common principles will enable co-operation between state institutions in evaluation of applications. Harmonised requirements will facilitate and simplify the application process for the applicants.

2. Preparation of the application

The guideline assumes that a 'desk-top' economic analysis in support of the application will be carried out for the purposes of the application, using data that are available from clinical trials or other valid studies, cost information and other data as appropriate. This type of analysis should be distinguished from a 'field' analysis, where a specially designed economic study is carried out for the specific purpose of supporting a listing application.

Any qualified person can carry out these analyses. The person who prepares the analysis (performer) must be identified in the submission and the relationships between the performer and the contractor must be clearly stated. If the economic analysis has been performed abroad, it could be applied to the local situation if necessary and appropriate adjustments have been done. Economic analysis will only be performed on the basis of published clinical trial data showing the therapeutic or therapeutic added value of a drug or on clinical trial data as yet unpublished but performed as part of the drug licensing process.

3. Study perspective

All analyses are to be conducted principally from a health care perspective (including only direct health care costs and benefits for healthcare).

Analyses from a societal perspective (including all costs and benefits outside the healthcare system) may only be presented in addition, if considered relevant by the applicant.

4. Analysis design and research question

The research question being addressed in the analysis and the economic importance of the research question should be stated.

5. Indications

Pharmacoeconomic analyses are to be performed for the indication(s) of a drug as approved in the respective states. The analysis should be performed on the entire population included in the clinical trial used and include all additional trial data that has addressed the study question. Presentation of the trial data should include indication of the original primary and secondary outcomes examined, and the clinical results achieved for those analyses. Subgroup data may be presented additionally in case of potentially important differences in clinical effectiveness or costs. If so, a justification for such analysis based on the complete trial population must also be presented.

6. Selection of alternatives

In the study the costs and outcomes of a standard treatment or the usual treatment in daily practice in the respective states should be compared with the costs and outcomes of the new drug.

If the new drug belongs to an existing pharmaco-therapeutic group, the comparator should be the most commonly used alternative drug within this group. If the new drug belongs to a new pharmaco-therapeutic group, the comparator should be the most commonly used alternative drug for the indication.

In addition, non-medicinal treatments or no treatment may be used as a comparator when they are the most commonly used practice.

Doses and duration of comparative treatments should preferably be those recommended in the summary of product characteristics and treatment guidelines as optimal for the relevant indication. If trial based dose comparisons are used, differences should be justified.

Choices of the alternatives must be justified.

7. Type of the pharmacoeconomic analysis

The type of the pharmacoeconomic analysis should be indicated.

The following economic evaluations can be conducted:

- Cost minimization analysis
- Cost effectiveness analysis
- Cost utility analysis (only additionally to the cost effectiveness analysis).

Cost minimization (CMA) analysis is applied if the therapeutic value of the new drug is equal to that of the comparator assuming that if the outcomes of the both treatments are equal, then only costs are compared.

Cost effectiveness analysis (CEA) compares different costs and different outcomes of two or more alternative treatments each with a common objective. Outcomes are measured in physical units. The objective of the cost effectiveness analysis is to

calculate the cost per unit outcome achieved using the incremental cost effectiveness ratio (ICER). This ratio relates the additional (incremental) benefits to the additional costs.

Cost utility analysis (CUA) is a more comprehensive (specific) form of CEA. CUA is performed from the societal perspective. Recommended outcome measure is quality adjusted life year (QALY), used to calculate the cost per unit outcome achieved incorporating patient preferences (utilities). Origin of the utilities used in the analysis should be explained and the instrument, whether generic or disorder-specific, used for measurement of quality of life has to be validated. It is recommended to use the EuroQol and the Health Utility Index methods.

Selection of the type of analysis should be justified.

8. Assessment of outcomes

The outcome indicator is the improvement in health resulting from the therapy. The final outcome is the change in the health state:

- prevention of death
- reduced incidence of complications
- reduced incidence of side-effects
- incidence of well controlled therapy symptoms, etc.

The basis for measurement of outcomes in economic analysis is randomised double blind controlled clinical trials, or open trials where these are appropriate. Adjustments to Baltic conditions and medical practice should be made, if the clinical trials have been performed in other countries. Points to consider include, but are not limited to:

- choice and frequency of other prescribed drugs or interventions
- patient age and sex distribution
- patient disease severity.

The key parameters of the clinical trials used include:

- explicitly stated study design
- clear statement of research question
- comparable patient groups at baseline
- clinically relevant endpoint and study duration
- "intention to treat" analysis
- the clinical and statistical significance of the achieved outcomes.

The economic analysis can be based on a single clinical trial or meta-analysis. Meta-analysis increases the precision of the estimates of differences between the new drug and comparator drugs. In case of meta-analysis details of study selection and statistical tests used should be indicated.

The results of clinical trials should be presented as a summary of outcomes for the new drug and the comparative therapies. For each comparison group the summary includes:

- the number of patients assigned to treatment
- the number of withdrawals
- the number of successes and failures (indicating the confidence intervals)
- changes in the mean values for the group (indicating the confidence intervals).

To identify the differences in the clinical effectiveness of the new drug and comparative treatments, absolute risk difference is calculated and used for

pharmacoeconomic analysis. Relative performance measures should also be provided.

9. Cost identification

If the economic analysis is performed from the health care perspective, all direct costs inside the health care system should be considered.

Direct health care costs may include:

- drugs (direct costs of treatment and of drugs used to treat side effects)
- medical services including procedures
- hospital services
- diagnostic and investigational services
- any other direct medical costs.

If additional economic analysis is performed from the societal perspective, other non-medical costs can be included (both direct and indirect costs outside the health care system):

- costs of social services
- patients' travelling expenses
- other costs to the patient or family.

If any direct or indirect costs outside the health care system are included, these should be indicated separately and calculations conducted separately (three analyses: one with direct costs inside the health care system, second with direct costs outside the health care system, third with additional costs outside the health care system).

Costs should be adapted to the local health care circumstances. Sources of data used to estimate costs should be provided.

The following identification and changes should be made:

- changes in the identification of resources. Not all costs measured in the clinical trial have to be identified, only those relevant to actual practice
- changes in the number of resources in natural units (number of consultations, number of bed days, etc.)
- changes in the cost per unit of resources.

All costs should be reflected in local currency.

10. Summary data presentation

Incremental analysis should be reported, comparing the relevant alternatives. The costs of treating patients in the comparison groups divided by the units of outcome achieved should be reported, that is – a cost per unit outcome of the new drug and alternative treatment should be reported (e.g. cost per death avoided).

To obtain the evidence of the differences in costs to achieve an extra unit of benefits, incremental cost effectiveness ratio (ICER) in CEA is calculated. The ICER shows the difference between the net direct costs and outcomes in comparison groups.

The analysis must also provide the estimate of the total annual cost of the treatments to the health care system and total benefit. Cost savings in the health care system should be presented, if relevant.

11. Discounting of costs and benefits

Discounting of future costs and benefits is a standard feature of economic evaluations. Costs and benefits distributed over time are discounted at an annual rate of 5 per cent. If other discounting rate is used, justification has to be provided.

12. Sensitivity analysis

A sensitivity analysis is a test used to measure the extent the results and outcomes of a study depend upon any assumptions. The sensitivity analysis has to be carried out and details should be given of the statistical tests performed and the confidence intervals around the main variables.

13. Modelling

If the analysis cannot be performed otherwise, modelling techniques can be applied (e.g. to model a sufficient analysis period when trial data provide too short a time frame, or when the data originate from a study which was carried out in another country with a different health care system). The model should be presented in a manner which will enable the replication of the analyses, electronic copy of the spreadsheets or the software used to generate the model should be submitted. Decisions on the use of effectiveness and resource estimates need to be substantiated. The basis for the model should be the state of scientific knowledge at the time that the study was performed.

References used in the preparation of the guideline:

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6. Drummond MF, Jonsson B, Rutten FFH. The Role of economic evaluation in the pricing and reimbursement of medicines. *Health Policy* 1997; 40: 199-215
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