**Cover**


**Research Center for Clinical and Economic Evaluation and Pharmacoeconomics of the Russian State Medical University named after N. I. Pirogov**

# PROTOCOL

## PROCEDURE FOR CLINICAL AND ECONOMIC EVALUATION OF DRUG LISTS THAT ARE SUBMITTED FOR REIMBURSEMENT COVERAGE FROM PUBLIC HEALTH CARE BUDGET. DECISION-MAKING CRITERIA

**(DRAFT)**

**Moscow**

**2010**

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**«Approved»**
**Chancellor of RSMU**
**named after N.I. Pirogov**
**Volodin N.N.**
**Protocol of the meeting of**
**Academic Council**
**No _____**
**_____ _____ 2010**

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**(DRAFT)**

### Development center:

**Research Center for Clinical and Economic Evaluation and Pharmacoeconomics of the Russian State Medical University named after N.I. Pirogov (Educational Institution of Higher Professional Training RSMU of Federal Agency for Public Health and Social Development)**

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# Moscow

## 2010

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# Contents

## 1. Field of application

These regulations contain requirements for developing draft lists of drugs that are submitted for reimbursement coverage from public health care budget. The requirements concern:

- Presentation of data on clinical efficacy, safety and economic acceptability of drugs
- Procedure of clinical and economic evaluation of drugs
- Criteria for assessment of data on clinical efficacy, safety and economic acceptability of drugs.

## 2. Goals and objectives

Goal: To determine scientifically grounded requirements for formation of drug lists.

Objectives:

- To determine requirements for presentation of data on clinical efficacy, safety and economic suitability of drugs for developing drug lists
- To determine requirements for presentation of data on disease epidemiology and real practice of patient management for developing drug lists
- To determine procedure of clinical and economic evaluation of drugs for developing drug lists
- To determine decision-making criteria for inclusion/non-inclusion of drugs into, or exclusion of drugs from, lists.

## 3. General provisions

3.1. Lists should be formed on the results of clinical and economic evaluation of drugs.

3.2. Clinical and economic evaluation of drugs should be conducted by a specially made authorized expert body.

3.3. Drug can be declared for inclusion into lists only if they are registered in the Russian Federation (RF) in accordance with the procedure established by RF legislation.

3.4. Every player of the medicine circulation process can be an applicant for inclusion of drugs into, or exclusion of drugs from, lists, including representatives of pharmaceutical companies, expert community, research institutes and medical institutions.

3.5. Examination of drugs is made by expert body and consists of 3 steps:

- Clinical evaluation of drugs
- Economic evaluation of drugs
- Recommendations of expert body for inclusion/non-inclusion of drugs into, exclusion of drugs from, lists that are based on the results of clinical and economic evaluation.

3.6. Meetings of expert body are held as necessary.

3.7. Approximate membership of expert body includes: a chairman, a vice chairman, members, and a secretary. The chairman directs the activity of expert body, fixes meeting dates, organizes work of expert body, allocates duties between members, and takes the chair at meetings of expert body. If the chairman is absent all his/her duties are performed by vice chairman. Members of expert body participate in meetings of expert body and take part in evaluation of a drug. The secretary maintains clerical work of expert body, prepares an agenda, projects of decisions and protocols of meetings of expert organ.

3.8. The meeting of the expert body is competent if not less than 2/3 of its members are represented. If an expert has no opportunity to attend meeting, he/she should inform the chairman of expert body about his/her opinion on concerned problem in writing not less than 3 days before meeting.

3.9. Recommendations for inclusion/non-inclusion of drugs into, exclusion of drugs from, lists are accepted by 2/3 of votes with open individual voting of members of expert body, taking into account opinions of absent members in writing.

3.10. Recommendations of expert body are put down into a protocol of the meeting (Appendix 1).

# Requirements for presentation of data

## 4. Requirements for presentation of data on clinical efficacy and safety of drugs

4.1. Data on drug efficacy and safety should be provided on the basis of results of clinical studies. The applicant should provide all available results of clinical studies for evaluation. The results of randomized controlled clinical studies and meta-analyses are preferable. Data on drug safety are provided on the basis of results of clinical studies and data from national and foreign pharmacovigilance systems (data from centres of drug monitoring that carry out pharmacovigilance).

4.2. The results of clinical studies should be presented as copies of reports and/or published articles. The applicant should estimate the level of evidence of drug efficacy of each study presented for evaluation (Appendix 2). Levels of evidence of drug efficacy can be modified during evaluation. Information about sponsors should be specified after each study.

4.3. If a drug submitted for inclusion in reimbursed lists and drugs that are already included into lists belong to the same ATC group, have the same therapeutic action and chemical structure, it is preferable that clinical studies that compare these drugs are provided.

4.4. In case drugs submitted for inclusion in reimbursed lists are innovative or do not have analogs with the same therapeutic action among those which are already included into lists, the comparator drug is chosen by the applicant.

4.5. If a drug submitted for inclusion in reimbursed lists is generic, it is necessary to provide manufacturer's GMP certificate as well as data on bioequivalence of the generic and original drugs. If manufacturer does not have GMP certificate, results of studies that confirm bioequivalence and therapeutic equivalence of the generic drug and the drugs previously included into lists should be provided.

4.6. If a drug submitted for consideration is rare (orphan), and randomized controlled clinical studies have not been conducted, the results of uncontrolled clinical studies can be accepted, including small sample studies.

4.7. The results of clinical studies should be provided as a summary with the following structure: name, authors, investigator sites, design, investigational nosology, comparator drug, criteria for efficacy assessment, results (figures), conclusions, sponsors. Full text reports and/or articles on clinical studies should be provided as an attachment to the application for drug listing.

## 5. Requirements for presentation of data on epidemiology of disease and real practice of patient management

5.1. When a drug is submitted for evaluation, data on epidemiology of disease for which the drug is intended as well as data on real practice of patient management should be provided.

5.1.1. Data on epidemiology of disease should be provided on the basis of state statistical observation, other official sources and epidemiology studies.

5.1.2. Data on real practice of patient management should be provided on the basis of patient registries and/or analysis of original medical records and/or interview of professionals (experts) in that field of medicine.

## 6. Requirements for presentation of data on economic acceptability of drugs

6.1. Data on economic acceptability of drugs should be provided on the basis of results of national clinical and economic (pharmacoeconomic) studies and cost of disease analysis. The results of foreign clinical and economic studies cannot be sufficient ground for acceptability of medical technology use in RF.

6.2. Cost-minimization analysis, cost-effectiveness analysis, cost-utility analysis, and cost-benefit analysis can be considered as the main types of clinical and economic analysis. Disease cost analysis and budget impact analysis can be considered as additional types of clinical and economic analysis. The type of clinical and economic analysis depends on the aim and position of the study, investigational drug, and final clinical result of its use. The choice of type of analysis should be explained by the applicant.

6.3. Clinical and economic studies provided for evaluation should have clearly-worded position defining whose economic interest associated with use of drug was taken into account. Clinical and economic studies can be conducted from the position of society (all costs associated with use of drug are taken into account); public health system at the federal level, at the level of RF subject, or municipality (only costs of public health system of appropriate level are taken into account); particular institution that provides medical aid or is responsible for its organization and financing (only costs of medical institution, medical insurance fund, medical insurance institutions, or health workers that undertake private-practice, etc. are covered); individual patient or his/her family (only costs that are paid by patient or his/her family are covered). When drugs are submitted for evaluation before inclusion into reimbursed drug lists, it is optimal to provide results of clinical and economic studies which have been conducted from the position of the society as a whole or the public health system in particular.

6.4. All clinical studies which resuts were taken as a basis for clinical and economic evaluation should undergo clinical evaluation (see items 4 and 7).

6.5. Final clinically significant criteria for assessment of outcomes are recommended for conduct of clinical and economic studies (survival, frequency of serious complications, frequency of hospital

admissions, life years gained, quality adjusted life years, and others). If such data are missing, intermediate (surrogate) criteria can be used with explanation.

6.6. Selection of a comparator drug should correspond to goals and objectives of the study. The choice of a comparator drug for clinical and economic analysis should be explained by investigator.

6.7. Studies which compare investigational drug with drugs which are already included into lists are given more value from the standpoint of clinical and economic assessment. If there are no such drugs in the reimbursed lists at the time when assessment is conducted, submitted drug can be compared with the most common drug with similar indications (typical pratice of management of a patient with that disease); the most effective drug among drugs with similar indications (efficacy should be confirmed in high-quality clinical studies); the cheapest drug among drugs with similar indications. Comparison with the absence of treatment is acceptable, if the latter exist in real practice of public health. As a rule, such a comparison is not an appropriate alternative for clinical and economic review.

6.8. Clinical and economic studies provided for evaluation should contain sources of data on costs. Sources of data on costs should be chosen according to the position of study, level of list which the drug is submitted for inclusion, and predominant practice of treatment for disease. Official sources of data on rates for services of public health system are preferable. Official registered prices adjusted for regional mark-ups, retail prices for medicines with analysis of expenses for out-patient treatment, and wholesale prices with analysis of expenses for in-patient treatment should be used for estimation of medicine cost.

6.9. Clinical and economic studies provided for evaluation can be conducted with use of the following types of design: prospective, retrospective, and simulation studies. The results of simulation of clinical and economic studies should be presented taking into account the following requirements: the model should be described in detail , open for evaluation and should correspond to real practice of patient management in RF. Approved standards, records, and recommendations can be considered as additional sources of data. Sensitivity analysis should be done and discount coefficient should be determined.. (If the technology is used more than one year, its costs should be discounted. Discount coefficient is substantiated by the applicant. Recommended discount coefficient is 5% per year)..

6.10. In the drug listing application, the results of clinical and economic studies should be provided as a summary with the following structure: name, authors, investigator sites, design, position, nosology, comparator drugs, sources of data on costs and types of costs, sources of data on efficacy and/or safety, tabulated results (Appendix 3), conclusions, sponsors. Full text reports and/or articles on clinical and economic studies should be provided as an attachment to the summary.

## 7. Procedure of clinical evaluation of drugs

7.1. Clinical evaluation is the first step of drug evaluation. Preparation of preliminary conclusion is the result of clinical evaluation (Appendix 4).

7.2. Clinical evaluation aims to assess the level of credibility of data on clinical efficacy and safety of drug.

7.3. Clinical evaluation includes evaluation of clinical studies and analysis of real practice of patient management as well as evaluation of bioequivalence and therapeutic equivalence studies if necessary.

7.4. When conducting clinical evaluation, experts who recommend inclusion/non-inclusion of drugs into, exclusion of drugs from, lists should follow principles of evidence-based medicine and find out whether the drug corresponds to the aims of list and is included into standards, clinical recommendations, and other drug lists.

7.5. When conducting drug evaluation, experts should not only analyze data provided by the applicant, but they should also search for clinical studies on their own.

7.6. When conducting drug evaluation, experts should analyze quality of clinical studies using formalized scales (Appendix 5). When conducting evaluation of clinical studies, experts can use scale of *levels of evidence* of drug efficacy for assessment of quality of an individual study (Appendix 2) and scale of *levels of credibility* of evidence of drug efficacy for assessment of the group of studies for the same drug (Appendix 6). The scale of *levels of credibility of evidence* of drug efficacy is used for final conclusion about drug efficacy. The expert should give one of three *levels of credibility* to received evidence. Consistency between the scale of *levels of evidence* and the scale of *levels of credibility of evidence* is presented in Appendix 7.

7.7. Experts should determine the level of evidence or confirm the one reported by the applicant and appoint the level of credibility of evidence of drug efficacy.

7.8. Assessment of social significance of disease, determination of possible use of drug in real practice, and forecast of costs for drug listing are the results of analysis of epidemiological data, data on real practice and cost of disease for which the drug is intended.

## 8. Procedure of economic evaluation of drugs

8.1. Economic evaluation is the second step of drug evaluation. Preparation of preliminary conclusion is the result of economic evaluation (Appendix 8).

8.2. Economic evaluation aims to assess the quality of provided clinical and economic studies and validity of economic justifications for drug listing.

8.3. Economic evaluation includes evaluation of validity of choice of type of clinical and economic analysis; clinical data and criteria for assessment of efficacy underlying clinical and economic study; presence of data on position of the study; validity of choice of comparator drug; validity of choice of source (-s) of data on costs; design of the study; results of the study.

8.4. When conducting drug evaluation, experts should not only analyze data provided by the applicant, but they should also search for clinical studies on their own.

## 9. Decision-making criteria for inclusion/non-inclusion of drugs into, or exclusion of drugs from, lists

9.1. Evidence of drug efficacy and safety, therapeutic equivalence and/or bioequivalence for generic drugs, potential demand of population for drug, and consistency with the aims of the list are criteria for positive preliminary conclusion of clinical evaluation.

9.2. When assessing clinical efficacy of drug, A and B levels of credibility of evidence of drug efficacy are criteria for positive preliminary conclusion for inclusion of the drug into lists. After the drug is given A or B level, it is provided for evaluation. Drugs with C level are not recommended for inclusion into lists. They are recommended for exclusion and economic evaluation is not conducted.

9.3. If necessary data on drugs are missing or incomplete at the time when assessment is conducted, expert body has the right to refuse an application until all necessary data will be provided.

9.4. If several submitted drugs have the same clinical efficacy,preference is given to drugs that have been investigated in randomized controlled clinical studies.

9.5. Drugs manufactured by foreign companies are not recommended for inclusion into lists without GMP certificate.

9.6. Evidence-based data on clinical and economic acceptability of drug and accordance between cost estimates and aims of list are criteria for positive preliminary conclusion of economic evaluation of drug.

9.7. Final decision of expert body is based on the results of clinical and economic evaluation as well as on social significance, cost and real practice of treatment of disease.

## 10. Terms and definitions

- **International Nonproprietary Name** (INN) is the name given to a pharmaceutical substance, as designated by the World Health Organization (Federal Law of RF No 61-FZ “On the Circulation of Medicines” dated April 12, 2010).
- **Trade name** is the name given to a medicine, as appropriated by its developer (Federal Law of RF No 61-FZ “On the Circulation of Medicines” dated April 12, 2010).
- **Medicines** are substances or their combinations that contact with, and penetrate into organs and tissues of, human or animal bodies; that are used in the prevention, diagnosis (excluding substances or their combinations that do not contact with human or animal bodies), or treatment of disease, rehabilitation, maintenance of pregnancy, prevention of pregnancy, or abortion; that are derived from blood, plasma, organs, and tissues of human or animal bodies, plants, and minerals with synthesis or biological technologies. Pharmaceutical substances and drugs are medicines (Federal Law of RF No 61-FZ “On the Circulation of Medicines” dated April 12, 2010).
- **Drugs** are medicines used in the prevention, diagnosis, or treatment of disease, rehabilitation, maintenance of pregnancy, prevention of pregnancy, or abortion (Federal Law of RF No 61-FZ “On the Circulation of Medicines” dated April 12, 2010).
- **Innovative medicine** is a new active substance or known pharmacological product with a new indication (EMEA).
- **Original medicine** is a medicine that contains new pharmaceutical substance or new combination of pharmaceutical substances. Efficacy and safety of the substances should be confirmed in preclinical and clinical studies (Federal Law of RF No 61-FZ “On the Circulation of Medicines” dated April 12, 2010).
- **Generic medicine** is a medicine that contains the same pharmaceutical substance or combination of pharmaceutical substances in the same formulation as original medicine and tha came into the market after the original medicine (Federal Law of RF No 61-FZ “On the Circulation of Medicines” dated April 12, 2010).
- **Biological medicines** include immunobiological medicines manufactured with biotechnological processes using recombinant DNA technology, controlled genes expression which encodes biologically active proteins, hybrid and monoclonal antibodies method as well as gene-therapeutic and somatic therapeutic medicines [ European Medical Agency (EMEA)]
- **Biosimilar** (generic biological drug) is a biological drug that came into the market after the term of validity of patent rights for original biological drug had expired. Biosimilars cannot be exact copies of original drugs and significantly differ from them in the structure of molecule,

biological activity, efficacy, and immunogenicity because exact reproduction of technology is impossible.

- **Therapeutic equivalence of medicine** means similarity of therapeutic effects of non-analogous medicines with similar therapeutic action ("Protocols for patient's management. General principals. GOST R 52600-2006", approved by the Federal Agency on Technical Regulation and Metrology Order No 288-ST dated 05/12/2006).
- **Bioequivalence of medicine** is the result of comparative bioavailability study of a drug with reference drug having the same International Non-proprietary Name (analogue) in bioequivalence studies ("Protocols for patient's management. GOST R 52600-2006" Approved Federal Agency on Technical Regulation and Metrology Order No 288-ST dated 05/12/2006)).
- **Bioequivalence study** is a type of clinical study that aims to determine the rate of absorption and excretion of pharmaceutical substance and quantity of pharmaceutical substance reaching systemic blood circulation and allow making a conclusion about bioequivalence of generic drug with specific formulation and dosage to the corresponding original drug (Federal Law of RF No 61-FZ "On the Circulation of Medicines" dated April 12, 2010).
- **Therapeutic equivalence study** is a type of clinical study that aims to reveal identical properties, safety and efficacy indicators and clinical effects of different drugs with the same formulation (Federal Law of RF No 61-FZ "On the Circulation of Medicines" dated April 12, 2010).
- **Drug effectiveness** refers to a degree of benefit of drug for progression, duration, and prevention of disease, rehabilitation, pregnancy preservation,, prevention or abortion (Federal Law of RF No 61-FZ "On the Circulation of Medicines" dated April 12, 2010).
- **Medicine safety** is a property of a drug based on the analysis of its efficacy versus risk of causing damage to health (Federal Law of RF No 61-FZ "On the Circulation of Medicines" dated April 12, 2010).
- **GMP** (Good Manufacturing Practice) is a system of norms, regulations and guidelines governing manufacture of medicines, medical devices, diagnostics, food products, dietary supplements, and active pharmaceutical ingredients.
- **Rare medical technology** is a type of medical technology that is applied or should be applied to less than 10000 people in the Russian Federation.
- **Evidence-based medicine** is a method of decision making in medicine, science, and expert evaluation which requires honest, precise, and intelligent application of the best results of clinical studies.

- **Cost-effectiveness analysis** is a form of clinical and economic analysis that compares costs and outcomes of two or more technologies with different effectiveness, however using the same parameters for assessing results (frequency of recovery or remission, number of prevented complications, life years gained, etc.).
- **Cost-minimization analysis** is a special instance of cost-effectiveness analysis.which is used to compare two or more technologies of equal efficacy and safety profile, but different costs. Cost-minimization analysis is recommended for comparison of different forms or different application conditions of one medicine or medical technology.
- **Cost-utility analysis** is a special instance of cost-effectiveness analysis that aims to assess the results of technology use in utility units from the point of view of consumer of medical assistance using integral indicator – "quality adjusted life year" (QALY).
- **Cost-benefit analysis** is a form of clinical and economic analysis where costs and results of technology use are expressed in money terms.
- **Discounting** refers to introduction of correction factor for cost estimation and sometimes for assessment of effectiveness taking into account the impact of time factor: future costs are less significant than today's costs and today's benefit is more significant than future benefit.
- **Sensitivity analysis** refers to determining the degree of change of study results taking into account variation of initial parameters (drug prices, frequency of side-effects, etc.).

**Appendix 1**

# Protocol of the meeting of expert body

No_____ Date _____ Moscow (city)

**Chairman** - Name
**Secretary** - Name

**Present:** Names.
**In attendance:** Names, positions.

**Agenda**

1. About …….
   The report of expert (name).

2. About …….
   The report of expert (name).

**1. PRESENTATION:**
Name – key-notes of the report.
**SPEAKERS:**
Name, position – key-notes of the speech.
Name, position – key-notes of the speech.
**DECISIONS:**
1.1. To approve …….
1.2. To submit …….

**2. PRESENTATION:**
**SPEAKERS:**
Name, position – key-notes of the speech.
Name, position – key-notes of the speech.
**DECISONS:**
2.1. To approve …….
2.2. To submit …….

**Chairman** Signature Name

**Secretary** Signature Name

**Appendix 2**

## Levels of evidence of drug efficacy

| Credibility of data | Studies | Level |
|---|---|---|
| The most credible data | Systematic reviews and meta-analyses | I |
| ↓ | Randomized clinical studies | II |
| ↓ | Quasi-experimental studies [1] | III |
| ↓ | Cohort studies | IV |
| ↓ | Case-control studies | V |
| The least credible data | Case reports, case series | VI |
| | Expert opinion | VII |

*Note.* The level of evidence is used for assessment of quality of an individual clinical study. The drug can be investigated in several clinical studies, and they can have different levels of evidence depending on their design.

[1] A quasi-experimental design is a type of study plan that due to lack of complete control over variables provide insuffcinent ground for making conclusions about cause-effect relationships between those variables. ("Experimental and quasi-experimental designs for research", Cambell, D. T. & Stanley, J. C., 1966). For example, preliminary group

matching procedure is missing or "parallel control" with participation of a control group is replaced by comparison of repeated testing of group (-s) results before and after intervention. Particularly, inequality between comparator groups is a result of disruption of randomization procedure or impossibility of implementing such a procedure.

**Appendix 3**

## Presentation of results of clinical and economic studies

| Drug | Costs, roubles (discounted / non-discounted) | | Efficacy | CER* | ICER* |
|---|---|---|---|---|---|
| | Direct | Indirect | | | |
| Investigational drug | | | | | |
| Comparator drug | | | | | |

*Note: CER – cost-effectiveness ratio (or other analysis: CBR – cost-benefit ratio, CUR – cost-utility ratio, CMR – cost minimization ratio). ICER – Incremental Cost-effectiveness Ratio.

**Appendix 4**

**Form of preliminary conclusion about the conduct of clinical evaluation of drug**

**INN: _____**

**Trade name: _____**

**Number of evaluated clinical studies with level of evidence for each study (Appendix 2):**

**_____**

**Level of credibility of drug efficacy (Appendix 5): _____**

**GMP certificate availability: _____**

**Bioequivalence studies availability (for generic drugs):_____**

**Therapeutic equivalence studies availability (for generic drugs):____**

**Analysis of epidemiological data and real practice of patient management:_____**

**General conclusion about the drug** (please,outline the necessary and explain in short)**:**

1. The drug is subject to economic evaluation

_____

2. The drug is not recommended for inclusion into lists

_____

3. The application is refused until all necessary data will be provided

_____

**Date of evaluation: _____**

**Expert name (-s), signature (-s): _____**

**Appendix 5**

## Jadad questionary[2]

1. Was the study described as randomized (this includes words such as randomly, random, and randomization)? No +0 (go to item 2). Yes +1. Was the method of generating random numbers described? If yes, and it was *appropriate* (table of random numbers, computer-generated randomization, toss-up, minimization) +1. If the generating random numbers method was described, but it *was inappropriate* (alternate inclusion into groups, date of birth, medical history number) –1.
2. Was the study described as double blind? No +0 (go to item 3). Yes +1. Was the method of double blinding described? If yes, and it *was appropriate* (for example, identical placebo) +1. If the method was described, but *was inappropriate* (for example., using tablet in one group vs. injection in other) –1.
3. Was a description of trial participants dropouts provided? (dropout is determined by the number of participants who were initially included in the study but did not complete it or were not taken into consideration when the final data analysis was conducted. No +0. If yes, the number of dropouts in each group should be described as well as the reasons for dropouts; if no dropouts were registered, it should be clearly stated +1 The scores for each point are summed, the maximum score is 5.

[2] Jadad A.R., Cook D.J., Jones A., et. al. Methodology and reports of systematic reviews and meta-analyses: a comparison of Cochrane reviews with articles published in paper-based journals. JAMA 1998;280:278—80.; Jadad A.R., Moher D., Browman G.P., et al. Systematic reviews and meta-analyses on treatment of asthma: critical evaluation. BMJ 2000;320:537—40.

**Appendix 6**

## Levels of credibility of evidences of drug efficacy

A – Evidence is credible: strong evidence for proposed statement

B – Relative credibility: sufficient evidence for recommendation of that proposal

C – No sufficient evidence: insufficient evidence for recommendation, but recommendations can be given taking into account other circumstances

*Note.* Levels of credibility of evidence of drug efficacy are used for assessment of all available studies that investigated the same drug, thus it is an aggregate indicator which is obtained by summarizing the data on levels of evidence of individual studies of different quality.

**Appendix 7**

**Consistency between the level of credibility of evidence and the level of evidence of drug efficacy**

| Type of study | Level of evidence | Level of credibility of evidences | |
|---|---|---|---|
| Systematic review of randomized clinical trials (RCTs), several large RCTs with unequivocal results and low probability of error | I, II | A | Evidences are credible: strong evidences of proposed statement |
| Small RCTs with unequivocal results and low or moderate probability of error<br><br>Quasi-experimental studies with good comparator groups<br><br>Cohort studies or case-control studies with unequivocal results and low probability of error | II, III, IV, V | B | Relative credibility: sufficient evidences for recommendation of that proposal |
| Case reports, case series; expert opinion<br><br>Low-quality studies of any design | VI, VII<br><br>I-VII low-quality | C | No sufficient evidences: insufficient evidences for recommendation, but recommendations can be given taking into account other circumstances |

**Appendix 8**

**Form of preliminary conclusion about the conduct of economic evaluation of drug**

**INN: _____**

**Trade name: _____**

**1. Is the selection of the type of clinical and economic analysis appropriate?** *Please, outline the necessary* **Yes No**

_____

**2. Is the position of the study clearly stated?** *Please, outline the necessary* **Yes No**

_____

**3. Is the design of the study described?** *Please, outline the necessary* **Yes No**

_____

**4. Is the choice of the comparator drug proven?** *Please, outline the necessary* **Yes No**

_____

**5. Are the criteria for assessment of efficacy appropriate?** *Please, outline the necessary* **Yes No**

_____

**6. Are the sources of data on costs indicated?** *Please, outline the necessary* **Yes No**

_____

**7. In case a clinical and economic model has been developed, can that model be verified?** *Please, outline the necessary* **Yes No**

_____

**8. Was sensitivity analysis conducted?** *Please, outline the necessary* **Yes No**

_____

**9. Were the results of the study described according to Appendix 3?**

*Please, outline the necessary* **Yes No**

_____

**10. General conclusion about the drug** (please, outline the necessary and explain in short)**:**

1. Submit assessment and recommendation for inclusion _____
2. The drug is not recommended for inclusion into lists _____
3. The appraisal of a drug is denied until receipt of required complete data _____

**Date of evaluation: _____**

**Expert name (-s), signature (-s): _____**

**Cover 3**

**FOR NOTES**

*Protocol. Procedure of clinical and economic evaluation of lists of drugs that are submitted for reimbursement from public health care budget. Decision-making criteria are issued with the assistance of Abbott Products, one of the leading global health care companies.*