The critical appraisal checklist (by Inotai et al. 2012)

	Topic	# of items
1.	Economic Evaluation	80
1.1.	Filter Questions	2
1.2.	Research Question (relevance, comparator, financing protocol)	2
1.3.	Health Benefit	25
1.3.1.	Source of Scientific Evidence	7
1.3.2.	Evaluation of Relative Effectiveness in Case of Indirect Comparison	10
1.3.3.	Magnitude of Health Benefit	8
1.4.	Cost	8
1.5.	Time Horizon, Discounting	3
1.6	Decision Rule	3
1.7.	Sensitivity Analysis	6
1.8.	Alternative Sections for Methodology	22
1.8.1.	Cost-Minimization Analysis	3
1.8.2.	Cost Effectiveness Analyses	19
1.8.3.	Decision Tree Model	4
1.8.4.	Markov model	7
1.8.5.	Simulation model	8
1.9.	General Methodology: Adequacy and Transparency	5
1.10.	Interpretation regarding the Economic Evaluation	4
2.	Budget Impact Analysis	11
	Total checklist	91

STA process timelines

- 1. day: receiving submission
- -3. day: responsible reviewers
- -5. day: checking of submitted data and publications
- -8. day: request for substitution or clarification of problems
- 9-40. day: consultation with applicant (if necessary)
- 40. day: draft report
- 43. day: final report

Decision makers in Hungarian reimbursement process

- Ministry of Health (Secretary State of Health)
- Ministry of National Economy
- National Health Insurance Fund
- Health Technology Assessment Committee
- Professional Board (Professional College)
- Department of HTA

Effect of use of HTA

- Impact: support the decision making process
- Barriers:
  - tight budget
  - poor quality of evidence of effectiveness
  - reimbursement mechanisms
  - cultural/political factors

The team of the office

- Physicians
- Pharmacist
- Economists
- Engineers
- Technical assistant

Thank you for your attention!

GYEMSZI
National Institute for Quality- and Organizational Development in Healthcare and Medicines

Hungarian Pharmacoeconomic Guideline, Regulations and Decision Making Process in Hungary

Zoltán Huszti

25 November 2013

Content

I. Hungarian Methodological Guideline for Conducting Economic Evaluation of Healthcare Interventions

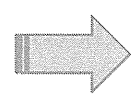
II. Major legal regulations of HTA in Hungary

III. Decision making process in Hungary

I.
Hungarian Methodological Guideline for Conducting Economic Evaluation of Healthcare Interventions

Background of the guideline development

- International trends
  - Increasing use of health economic studies in decision making word-wide
  - The need for countries to develop their own guidelines rather than use a global version
- Regulation environment
  - Reimbursement of pharmaceuticals should be based on cost-effectiveness analysis
  - Reimbursement system should take account of cost-effectiveness



Hungarian Methodological Guideline for Conducting Economic Evaluation of Healthcare Interventions

First version published in 2002

First in East Central Europe

- Based on international guidelines
- Consensus of experts from participating ministries, healthcare and academic institutions, consulting firms and pharmaceutical companies
- Suggestions from international experts

Content of the Guideline

- Preamble
- Implemented changes in the guideline
- Objective of the guideline
- Legal backgrounds
- Scope of the guideline
- List of contributors
- Short and detailed recommendations (12)
- References

Guideline recommendations

Guideline 1: description of healthcare interventions, patient population and the health service needs should be addressed in the analysis

Comparators: routine care

Guideline 2: analytic perspective

Primarily health care payer perspective

Guideline 3: type of economic evaluation

CMA, CEA, CUA , (CBA should not be used)

Guideline 4: measurement of health improvement – denominator of the cost-effectiveness ratio

- *Should be appropriate for the selected condition, and include final (long-term) outcome (morbidity, mortality)*
- *Direct comparisons are preferred against the indirect comparisons*

Guideline recommendations

Guideline 5: measurement of costs: numerator of the cost-effectiveness ratio

- *The perspective of costing should be the same as the study perspective.*
- *Cost analysis should consider only those costs that related to treatment (direct costs)*

Guideline group 6: handling time in economic evaluation studies

The time horizon of a study should be long enough to cover all significant clinical and cost consequences that are directly related to the healthcare intervention.

Discount rate for costs and outcomes is 3,7% (SA: 2%; 5%)

Guideline recommendations

Guideline group 7: synthesis of health gains and costs: presentation of results on final cost-effectiveness

Incremental cost-effectiveness and/or cost-utility ratio should be reported separately and aggregated.

Guideline 8: examining robustness and generalisability of study results

- *Deterministic and probabilistic sensitivity analyses is also recommended.*
- *Subgroup analysis is reasonable if a definite group of patients vary in efficacy or cost-effectiveness.*
- *Examination the internal and external validity of cost-effectiveness analysis and clinical studies is necessary*

Guideline recommendations

Guideline 9: impact on healthcare, expenditures and equity

Budget impact analysis is required, 3- to 5-year period should be discussed.

Guideline 10: Conclusions

Cost-effectiveness threshold: twofold and threefold of GDP per capita (5.600.000 – 8.400.000 HUF / QALY ~ 19.000 – 28.400 EUR / QALY)

Guideline 11: information on authors, sponsors, and competing interests

Guideline 12: reporting template

II.
Major legal regulations of HTA in Hungary

Legal regulations

Act 2006. XCVIII.

- *Drugs, nutrition, medical devices intended for patient use can be subsidized by the social insurance if the cost-effectiveness is certified*
- *The social insurance body exclude the drug from the social insurance system, if*

  the cost-effectiveness is questionable

  the budget of social insurance is disproportionately charged

  the cost-effectiveness is unverifiable

Legal regulations: Pharmaceuticals

32/2004. (IV. 26.) Decree of Ministry

Reimbursement principles:

- *Professional establishment: evidence based decision*
- *Considering the budget allowance, financing requirements*
- *Transparency*
- *Computability*
- *Publicity*
- *Transparency of interest*
- *Necessity based approach*
- *Cost-effectiveness*

Legal regulations: Pharmaceuticals

32/2004. (IV. 26.) Decree of Ministry

Reimbursement rules:

GYEMSZI examines the cost-effectiveness and budget impact of the product.

Process rules:

National Health Insurance Fund Administration (payer) sets up the Technology Assessment Committee

National Health Insurance Fund Administration (payer) makes the reimbursement decision after receiving the opinion of GYEMSZI and the competent medical professional college

If a new patient group or therapeutic indication seting up is necessary the minister of health can modify the decree in consent with the ministry of finance.

If the drug is reimbursed in an „itemized" way the minister of health makes the decision that based on a committee proposal.

Legal regulations: Medical Devices Intended for Patient Use

14/2007. (III. 14.) Decree of Ministry

Reimbursement principles:

- *Considering type of disability and disease*
- *Considering equity*
- *Necessity based approach*
- *Professional grounding*
- *Complexity*
- *Cost-effectiveness*
- *Considering budget impact*
- *Effectiveness*

hz2

Legal regulations: Medical Devices Intended for Patient Use

14/2007. (III. 14.) Decree of Ministry

Professional considerations:

… only those medical devices intended for patient use can be reimbursed which efficacy and cost-effectiveness are proven

Process rules: GYEMSZI critically evaluate the cost-effectiveness of the device

Legal regulations: Medical Devices

180/2010. (V. 13.) Decree of Government

GYEMSZI critically evaluate the cost-effectiveness of the device

28/2010 (V.12.) Decree of Ministry

Professional viewpoints of decree:

Severity of disease, public health priorities, size of patients population, etc.

… cost-effectiveness should be considered

31. dia

hz2 huszti.zoltan; 2013.10.03.

III.
Decision making process in Hungary

Decision making process in Hungary

Simplified procedure:

- new generics,
- …

Deadline: 60 days

Normal procedure:

- all new agents,
- …

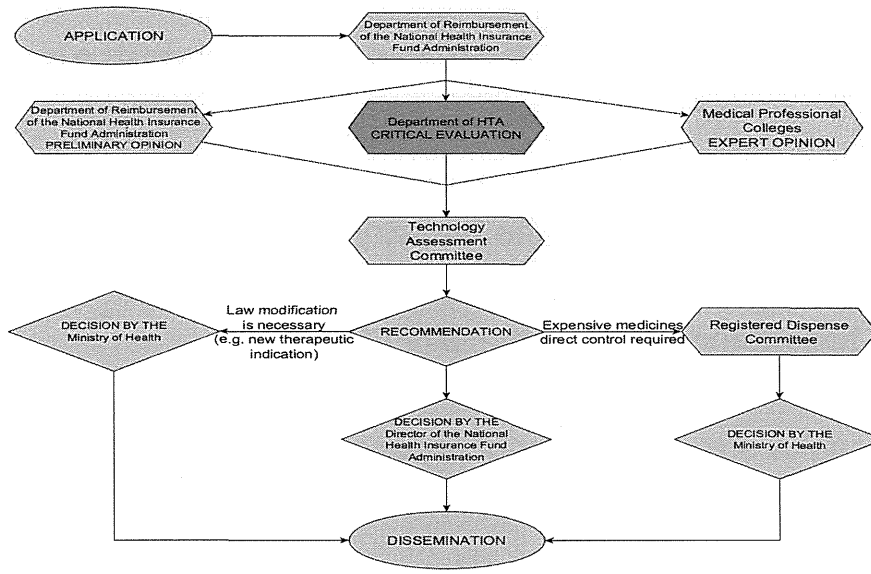
HTA is only necessary in this case

Manufacturers are obligated to submit clinical evidences and cost-effectiveness and budget impact evaluations.

Deadline: 90 days

GYEMSZI National Institute for Quality- and Organizational Development in Healthcare and Medicines

Decision making process (normal procedure)



Technology Assessment Committee

VOTING MEMBERS:

1. Chairman of Technology Assessment Committee (NHIFA)
2. Head of Reimbursement Department (NHIFA)
3. Deputy Head of Reimbursement Department (NHIFA)
4. Head of General Funding Department (NHIFA)
5. Head of Analysis, Medical Professional and Professional Controlling Department (NHIFA)
6. Hungarian Chamber of Pharmacists
7. Medical Professional Colleges Presidents Board
8. Medical Professional Colleges Presidency

ADVISORY MEMBERS:

1. Head of HTA Department (GYEMSZI)
2. Head of Pharmaceutics and Medical Device Department (Ministry of Health)
3. Head of Social Expenditure Department (Ministry of Finance)

Quorum: *attend at least 5 voting members*

Decision: *with at least 5 votes*

„Registered dispense" Committee

Two attendees from the Ministry of Health,
one attendee from the Ministry of Finance,
two attendees from the NHIFA,
two attendees from the GYEMSZI

make a reimbursement proposal for the Ministry of Health.

Thank you for your kind attention!

GYEMSZI
National Institute for Quality- and Organizational Development in Healthcare and Medicines

Medical aspects in HTA

Csenge Földesi

25.11.2013

Hungarian rules of procedures

Normal procedure

- New agent/molecule
- New indication
- New formula and new mode of administration
- Rise in price
- New combination
- Change in reimbursement category
- Everything not included in simplified proceeding

Simplified procedure

- New generic drug
- Equivalent to an already reimbursed drug
- New packaging
- New dose
- New formula and same mode of administration

„Classification" of medicines 1.

- **Innovative drugs** – „new" chemical entity
  - eg. new target therapy in oncology
- **Generic products** – essential similarity to the original
  - no bioequivalence trial – simplified procedure not applicable
- **Well-established use** – sufficient evidence in medical use for at least 10 years
  - rise in price
  - „old" molecule, not reimbursed in Hungary so far
- **Orphan drugs** – rare, life-threatening or chronically debilitating, <5/10.000
  - small No. of patients, expensive therapy

„Classification" of medicines 2.

- **Ultra-orphan drugs** – extremely rare, <1/50.000
  - very small No. of patients, extremely expensive therapy
- **Biosimilar products** – „highly similar" product to a biological (biotechnological) agent – „follow-on biologic"
  - simplified procedure not applicable
  - eg. insulin, erythropoietin, monoclonal antibody
- **Blood products** – e.g. factor VIII
- **Vaccination** – e.g. pneumococcal vaccine

Evidence requirements

Medicine	Evidence
Innovative drugs	Randomized, controlled, double-blind, multicentre phase III trials (RCT)
Generic drugs	Bioequivalence trial
Well-established use	Bibliographic scientific literature, meta-analysis, systematic reviews
Orphan (ultra-orphan) drugs	Not RCT (phase II/III), small patient No., surrogate endpoints
Biosimilar drug	Biosimilarity trials (no meaningful difference from the reference drug)

Main scopes of the medical evaluation

- Target population
- Therapeutic indication vs. reimbursement indication
- Place of the new therapy in the actual treatment algorithm
- Appropriate comparator
- Evidence (efficacy, safety)
- Relative effectiveness – comparator

Principles of the economic evaluation

- CHECKLIST – to check the pivotal issues of the submission

Demonstration of cost-effectiveness

Medical support

1. Cost-minimization analysis (CMA)
   - The new therapy and the comparator are equivalent in terms of efficacy AND safety
2. Cost-utility analysis (CUA) and cost-effectiveness analysis (CEA)
   - Are the data used in modeling appropriate from medical aspect?
     - » Result of the clinical trials
     - » Cost data
     - » Time period
     - » Model status
     - » Utility data (CUA)

Criteria of assessment

Support the decision making procedure

Criteria	Medical aspect
Budget impact	Epidemiologic data – No. of patient population, duration of treatment
Cost-effectiveness	Is the cost-effectiveness analysis adequate?
Patient benefit	Magnitude of health benefit
Acuity considerations	Pediatric patient population, orphan disease, first new treatment since decades
Therapeutic alternatives	Unmet medical need (best supportive care)
Public health impact	Burden of disease, vaccination
Innovative characteristics	Novelty of the new treatment

Overview of the medical sections of our evaluation

1. Background
   a) Introduction of the disease (burden, epidemiology, guidelines, comparator)
   b) Introduction of the drug (summary of product characteristics, side effects)

2. Summary of the main clinical trials
   a) Summary of evidences about the new drug
   b) Summary of evidences about the comparator
   c) Critics of the indirect comparison/meta-analysis

Epidemiologic data

- **Determine the number of patients who could benefit from the new therapy**
- **Budget impact**

- Hungarian prevalence/incidence data often missing/ out-of-date
- Hungarian **registry** are lacking
  - Oncology
  - Rare/orphan disease
  - Pediatric disease
- International (European/USA) data generally available
- *Are international epidemiological data relevant for Hungary?*