

COST-UTILITY OF AMISULPRIDE COMPARED WITH FIRST GENERATION ANTIPSYCHOTICS IN TREATMENT OF SCHIZOPHRENIA IN POLAND

Objectives

The aim of this economic analysis was to compare costs and effectiveness of amisulpride (Solian®) in the treatment of schizophrenia and to determine whether it is cost-effective option for schizophrenia patients in Poland.

Methods

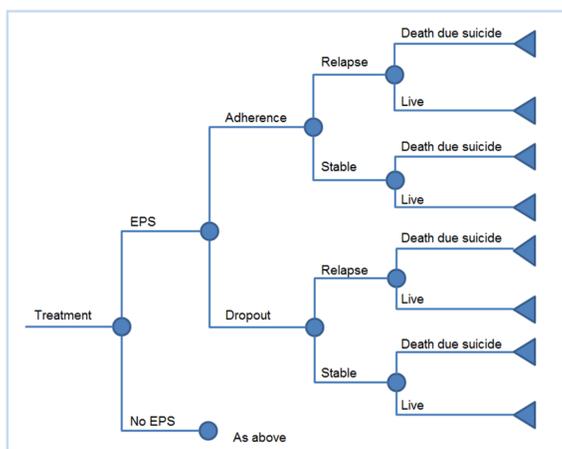
- Comparators for amisulpride (AMI) were first generation antipsychotics (FGA). The following drugs were considered: haloperidol (HAL), perazine (PER) and flupenthixol (FLU).
- Cost-effectiveness was analyzed in population of adults with schizophrenia.
- The analysis was conducted by developing a decision-tree model simulating the outcomes within the first year of episode of schizophrenia depending on treatment applied.
- Efficacy and safety of interventions were assessed based on the results of clinical trials identified by means of a systematic review. [1] The results of the review indicate that amisulpride is favourable to FGA in terms of several clinical outcomes: improvement of patients condition according to numerous quality of health state scales (CGI¹, BPRS², PANNS-N³, PANSS-P⁴, GAS/GAF⁵, MANSA⁶, FSQ⁷, SANS⁸, MS⁹, CDSS¹⁰, QLS¹¹) and reduction of adverse effects (total, adverse effects (AE) resulting in withdrawal, extrapyramidal symptoms (EPS), serious AE). As there was no reliable method to estimate the influence of most of those highly specific outcomes on costs and patient's health state utility only two parameters assessed in the systematic analysis were incorporated in the cost utility-analysis (CUA): probability that patient continues the initial treatment and risk of EPS. The other factors implemented in the model: probability of relapse for amisulpride or FGAs and risk of suicide were based on data from complementary publications. [2, 3] It was assumed that effectiveness and safety profile of all FGA are equal which is consistent with the inference from the systematic review. [1]
- The analysis was performed from the perspective of payer (National Health Fund and patients in case of co-payment). Costs were calculated on the basis of National Health Fund Data, surveys and literature. The following cost categories were taken into account in the analysis: 1) costs of drugs: amisulpride, haloperidol, perazine, flupenthixol and drugs used in case of schizophrenia relapse 2) costs of extrapyramidal syndrome management, 3) costs of psychiatric hospitalization, 4) costs of ambulatory visits. Units costs are presented in Table 2.
- The main outcome measures used in the economic analysis were costs of treatment and management and quality adjusted life years (QALYs). Incremental cost utility ratios (ICURs) were calculated and compared to polish acceptability threshold (ca 100k PLN/QALY or ca 25k EUR/QALY). In the probability sensitivity analysis (PSA) the likelihood of amisulpride being cost-effective was calculated.
- A one year horizon was adopted – the period for which clinical data were available. As schizophrenia is a chronic disease the observed differences between treatments may be therefore underestimated.
- Dosage of drugs was determined according to DDD for each drug. It was assumed, that patients defined as adherent took 87% of prescribed doses and that non-adherent patients receive 37% of prescribed medications. [4]
- It was assumed that in case of relapse patients are placed in the care of psychiatric ward – either a day ward (40%) or an all day care (60%). It was assumed that this stage of treatment lasts for 73 days [5]. It was also adopted that the second line treatment is based on an atypical antipsychotic – either risperidone (50%) or olanzapine (50%).
- Utility values were identified by means of a review of published data of schizophrenia modelling. In the main case scenario the utility value set was determined on the basis of data published in Davies 2004. It was conservatively assumed that the baseline utility is identical for treatment with both atypical and typical antipsychotic.
- Analysis was conducted according to Polish HTA agency guidelines.

Decision-tree

Decision tree structure comprises 4 possible treatment consequences, which probability depends on the drug choice: occurrence of extrapyramidal symptoms, discontinuation of therapy (non-adherence), relapse and suicide. The range of possible pathways is identical for patients on FGA and those who are treated with amisulpride. However, according to the data from systematic review [1] and other publications [2, 3] the chance of achieving desired treatment results is higher for those receiving atypical antipsychotic.

The applied time horizon is one year. Structure of the decision tree is presented on Figure 1 and the probabilities of transitions are summarized in Table 1.

Figure 1. Decision tree model



1 Clinical Global Impression
2 Brief Psychiatric Rating Scale
3 Positive and Negative Syndrome Scale – Negative Syndromes
4 Positive and Negative Syndrome Scale – Positive Syndromes
5 Global Assessment of Functioning
6 Manchester Short Assessment of Quality of Life
7 Functional Status Questionnaire
8 Scale for Assessment of Negative Symptoms
9 Manchester Scale
10 Calgary Depression Scale for Schizophrenia
11 Quality of life scale

Summary

OBJECTIVE: To evaluate cost-utility of amisulpride compared with first generation antipsychotics (FGA) in treatment of schizophrenia in adult patients in Poland.

METHODS: A decision-tree model was used to estimate utilities and costs of treatment of amisulpride therapy in comparison to FGA (antipsychotics, management of main antipsychotics' adverse events - extrapyramidal symptoms (EPS) and health care costs). The FGA group included the following drugs: haloperidol, perazine and flupenthixol. Analysis was performed from the National Health Fund (NHF) perspective with a time horizon of 1 year. The range of possible events in the model included: therapy discontinuation (regardless of reason), EPS occurrence, schizophrenia relapse and suicide. Range of events was assumed to be the same for amisulpride and FGA but probabilities of those events varied between antipsychotics. Based on systematic review of RCTs amisulpride is more effective than FGA in terms of compliance rate and in reduction of both the risk of relapse and occurrence of EPS. A probabilistic sensitivity analysis was performed to estimate the probability that amisulpride is cost effective in Polish conditions (threshold about 100,000 PLN/QALY).

RESULTS: From the NHF perspective amisulpride compared with FGA was more effective (Δ QALY = 0.004) and it was cheaper (comparing to flupenthixol) or cost-effective (ICUR=1 079 PLN/QALY and ICUR=31 810 PLN/QALY in comparison to haloperidol and perazine, respectively). The calculated probability that amisulpride is more effective than any of FGA was 100%, while the probability that it is also cost-effective varied between 68% for perazine to 83% for flupenthixol.

CONCLUSIONS: Treatment of schizophrenia with amisulpride is a cost-effective option in comparison to FGA in Poland. The obtained difference in QALY is very small, but reduced risk of relapse and necessity of hospitalization due to better effectiveness of amisulpride and reduced occurrence of EPS results in a better cost benefit outcome for amisulpride compared to FGA.

Results

The estimated clinical outcomes expressed in terms of QALY associated with amisulpride surpass those for FGA. The estimated difference in QALY between amisulpride and FGA is equal to 0.004 in one-year horizon (Table 4).

As well as clinical outcomes, the total costs are also very similar for amisulpride and FGAs. The estimated difference in total costs is less than 50 €. The one year therapy (drugs and management) with amisulpride is on average about 1-33 € more expensive than the therapy with haloperidol or perazine and it is about 49 € cheaper than a course based on flupenthixol. Almost equal cost of all treatment paths is a result of balancing the drug costs which are higher in amisulpride arm with the costs of hospital resources which are decreased when amisulpride is applied - reduction of calculated hospital costs in the first year costs is about 400 € per patient (Table 5, Figure 2).

ICUR for comparison amisulpride vs haloperidol is about 270 € and in comparison amisulpride vs perazine it is about 7 950 €. This value is much below the standard polish cost-effectiveness threshold (about 25 000 €/QALY). Amisulpride is dominant in comparison with flupenthixol (more effective and cheaper). Due to minimal differences within both clinical and economic outcomes ICURs should be interpreted only in reference to PSA outcomes (Figures 3-5). The results of PSA analysis support the conclusion of cost-effectiveness of amisulpride: calculated probability that the treatment analyzed is cost-effective (it is the probability that the incremental results are below the acceptability threshold) varies from 68% for perazine to 83% for flupenthixol. All simulations (100%) indicate the advantage of amisulpride in terms of clinical outcomes as expressed in QALY and about 40-60% of simulations indicate that it is dominant over its comparator.

Results of probabilistic sensitivity analysis are presented on Figures 3-6.

Table 1. Effectiveness parameters

| Parameter | Amisulpride | FGA | Source |
|--|-------------|-------|-----------------------|
| Treatment discontinuation | 34% | 54% | Systematic review [1] |
| EPS occurrence | 28% | 37% | Systematic review [1] |
| Relapse in case of patient's cooperation | 20% | 34% | Bagnall 2003 [2] |
| Relapse in case of lack of patient's cooperation | 75% | 75% | Bagnall 2003 [2] |
| Suicide in case of patient's cooperation | 0,12% | 0,12% | Davies 2004 [3] |
| Suicide in case of lack of patient's cooperation | 0,50% | 0,50% | Davies 2004 [3] |

Table 2. Unit costs

| Cost category | Value | |
|---------------------------------------|------------|--------|
| Drug (daily cost) | AMI | 2,08 € |
| | HAL | 0,23 € |
| | FLU | 0,46 € |
| | PER | 0,08 € |
| Hospitalization in case of recurrence | 2 202,79 € | |
| EPS management | 6,27 € | |
| Ambulatory visit | 15,90 € | |

Table 3. Utility parameters

| Parameter | Value |
|---|--------|
| Baseline utility of schizophrenia episode | 0,570 |
| Disutility associated with extrapyramidal syndromes | -0,060 |
| Disutility associated with relapse | -0,058 |

Table 4. Clinical outcomes – QALY

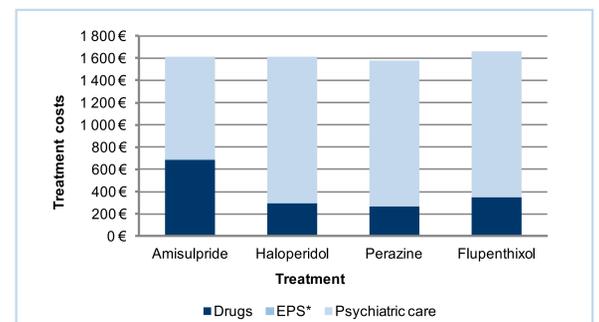
| Treatment | Value | Difference |
|-----------|-------|------------|
| AMI | 0,560 | - |
| HAL | 0,554 | 0,004 |
| PER | 0,554 | 0,004 |
| FLU | 0,554 | 0,004 |

Table 5. Economic outcomes

| Treatment | Drugs | Psychiatric care | EPS | Total | - |
|-----------|-------------------|------------------|-------|-----------|-------------------------|
| AMI | 688,8 € | 924,1 € | 1,7 € | 1 614,6 € | - |
| HAL | 297,0 € | 1 314,2 € | 2,3 € | 1 613,5 € | - |
| PER | 264,7 € | 1 314,2 € | 2,3 € | 1 581,2 € | - |
| FLU | 347,3 € | 1 314,2 € | 2,3 € | 1 663,8 € | - |
| | Difference | | | | Cost/QALY (ICUR) |
| HAL | -391,8 € | 390,1 € | 0,6 € | -1,1 € | 269,8 € (1 079 PLN) |
| PER | -424,1 € | 390,1 € | 0,6 € | -33,4 € | 7 952,5 € (31 810 PLN) |
| FLU | -341,5 € | 390,1 € | 0,6 € | 49,2 € | AMI is dominant |

*costs below the standard willingness to pay threshold (about 25 000 €/QALY)

Figure 2. Costs of treatments



*due to low costs of EPS management data are not visible (data in Table 4)

Figure 3. Scatter plot, amisulpride vs haloperidol

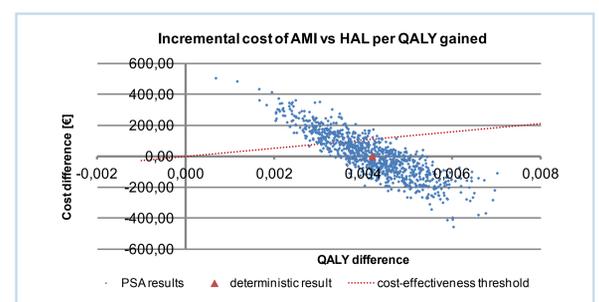


Figure 4. Scatter plot, amisulpride vs perazine

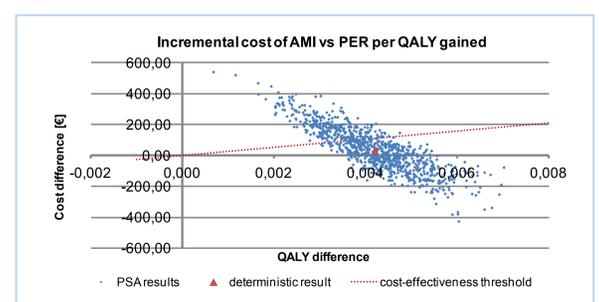
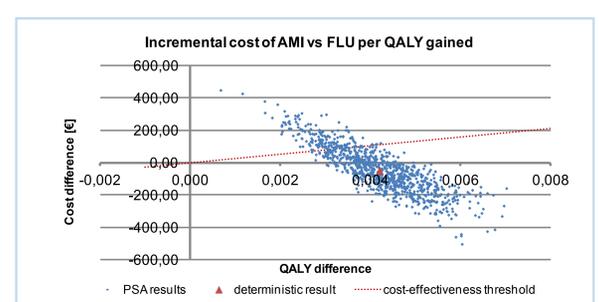


Figure 5. Scatter plot, amisulpride vs flupenthixol



Conclusions

Amisulpride is considered a cost-effective option for management of schizophrenia episode in comparison with first generation antipsychotics in Poland. Its clinical advantage accounts for the stable position of amisulpride in schizophrenia treatment and is a real value as it significantly broadens the range of therapy options for a demanding medical challenge. The higher price of drug is counterbalanced by the decreased resource usage related to superior efficiency and reduced occurrence of EPS.

References

- Siejka S, Ziola M, Kowalska M, et al. Analiza kliniczna amisulpridu (Solian®) względem opcjonalnych sposobów postępowania w terapii ostrej i przewlekłej schizofrenii z objawami pozytywnymi i/lub negatywnymi, w tym także schizofrenii z przewagą objawów negatywnych.
- Bagnall A-M, Jones L, Gimbley L, et al. A systematic review of atypical antipsychotic drugs in schizophrenia. Health Technology Assessment (Winchester, England). 2003; 7(13):1-193.
- Davies A, Schroyer R, Crowley S, et al. Economic analysis of risperidone long-acting injection in New Zealand. Economic analysis of risperidone long-acting injection in New Zealand. International Society for Pharmacoeconomics and Outcomes Research 7th Annual European Congress; październik 2004; Germany.
- Crowley S, Schroyer R, Neville A. Cost-effectiveness analysis of risperidone long-acting injection for the treatment of partially adherent patients with schizophrenia in Australia. Cost-effectiveness analysis of risperidone long-acting injection for the treatment of partially adherent patients with schizophrenia in Australia. International Society for Pharmacoeconomics and Outcomes Research 7th Annual European Congress; październik 2004; Germany.
- Instytut Psychiatrii i Neurologii. Zakłady psychiatrycznej i neurologicznej opieki zdrowotnej. Rocznik statystyczny 2007 Warszawa 2008.