ECONOMIC EVALUATION OF TIOTROPIUM ADMINISTRATED THROUGH THE RESPIMAT INHALER AS ADD-ON THERAPY IN PATIENTS WITH UNCONTROLLED SEVERE ASTHMA IN POLAND

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BACKGROUND

A considerable proportion of patients with asthma remain uncontrolled or symptomatic despite treatment with combination of high dose of inhaled corticosteroids and long-acting β2-agonists (ICS/LABA).

Currently, there are no other therapeutic options available for this category of asthma (GINA step 4-5), therefore patients must continue ICS/LABA therapy. Clinical trial data have shown that tiotropium as an add-on controller therapy on top of usual care versus usual care alone in adult patients with severe persistent asthma, leads to a reduction in severe exacerbations and to an improvement of asthma control.

OBJECTIVE

To assess a cost-utility of tiotropium administrated through the Respimat inhaler as the add-on controller therapy on top of usual care in patients with severe persistent asthma from both the public payer's and common (patient and National Health Fund - NHF) perspectives in Poland.

METHODS

The economic evaluation for tiotropium Respimat was performed in accordance with Polish HTA requirements.

Key features

Patient population	Adult patients with asthma, who are currently treated with the maintenance combination of inhaled corticosteroids (≥800 µg budesonide/day or equivalent) and long-acting β2-agonists (LABAs) and who experienced one or more severe asthma exacerbation in the previous year (GINA – Global Initiative for Asthma 4-5 step)
Intervention	Tiotropium (Spiriva® Respimat® 5 mcg) + SOC
Comparator	SOC (high dose ICS and LABA)
Outcomes	Mean costs per patient, QALYs, Costs per QALY gained (ICUR)
Model horizon	Lifetime
Cycle length	1 week
Perspective	The public payer's and common (patient and National Health Fund - NHF)
Cost assessment	Direct costs
Discount rate, costs	5% per year
Discount rate, effect	3.5% per year

Structure of the Markov model

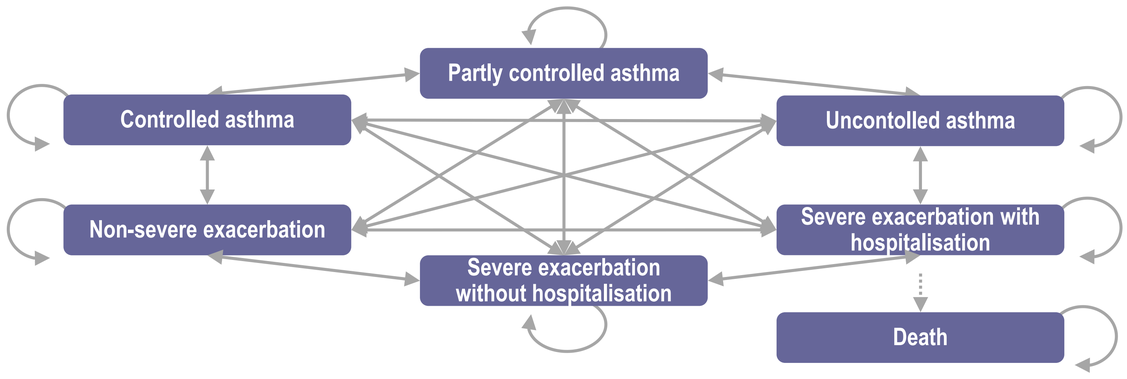
The Markov model was developed in TreeAge Pro 2014. The model structure was based on the model presented in the economic analysis Willson 2014 [1], which was a source of transition probabilities.

The model included seven mutually exclusive health states, which reflect the disease pathway (Figure 1):

- three asthma control health states (controlled asthma, partly controlled asthma, uncontrolled asthma),
- three exacerbation health states (non-severe exacerbation, severe exacerbation without hospitalization, severe exacerbation with hospitalization) and
- death.

It was assumed that at the beginning of the simulation the majority of patients are in the 'uncontrolled asthma' health state. No patients are in an exacerbation state at model start. With the exception of the absorbing state 'death', patients could transition back and forth between all states at the end of each cycle.

Figure 1. *Markov model structure*



Comparisons

The economic model compared the costs and health effects of tiotropium added to optimal standard of care (SOC) with SOC alone (high-dose ICS and LABA) over a lifetime horizon.

Results calculating

- The measure of effectiveness were quality adjusted life years (QALY)
- The incremental cost-utility ratio (ICUR) was determined from the following formula:

$$ICUR = \frac{Cost_{TIO+SOC} - Cost_{SOC}}{QALY_{TIO+SOC} - QALY_{SOC}}$$

Time horizon

The lifetime horizon (until the patient is over 100 years) was taken into account. The cycle length of the model was set as one week, which allows the necessary detail level for representation of the exacerbation events.

Inputs data

Treatment efficacy of tiotropium Respimat was defined as a reduction in exacerbations and an improvement of asthma control. The asthma control was defined using the Asthma Control Questionnaire (ACQ-6) scores. The transition probabilities matrices, determining to which health state a patient switches at the end of a cycle were retrieved from analysis published by Willson et al [1], in which the time dependence of effectiveness was taken into account by use of a two-phase transition matrix structure. Transition probabilities for 'early response phase' were derived from the pooled Primo-TinA-asthma trials [2] data. The matrices for 'late response phase' were computed using a WinBUGS model.

Table 1. *Model transition probabilities, TIO+SOC arm*

From \ To	Controlled asthma	Partly controlled asthma	Uncontrolled asthma	Non-severe exacerbation	Severe exacerbation - without hospitalisation	Severe exacerbation – with hospitalisation
"Early response phase"						
Controlled asthma	0.945	0.004	0.008	0.025	0.013	0.004
Partly controlled asthma	0.057	0.889	0.025	0.020	0.007	0.002
Uncontrolled asthma	0.018	0.022	0.930	0.021	0.008	0.000
Non-severe exacerbation	0.110	0.069	0.616	0.137	0.055	0.014
Severe exacerbation - without hospitalisation	0.041	0.042	0.417	0.042	0.437	0.021
Severe exacerbation – with hospitalisation	0.166	0.167	0.167	0.167	0.166	0.167
"Late response phase"						
Controlled asthma	0.954	0.019	0.010	0.010	0.007	0.000
Partly controlled asthma	0.029	0.913	0.033	0.019	0.005	0.002
Uncontrolled asthma	0.006	0.016	0.939	0.030	0.010	0.001
Non-severe exacerbation	0.081	0.092	0.576	0.237	0.009	0.004
Severe exacerbation - without hospitalisation	0.097	0.078	0.292	0.019	0.510	0.004
Severe exacerbation – with hospitalisation	0.062	0.125	0.281	0.063	0.031	0.438

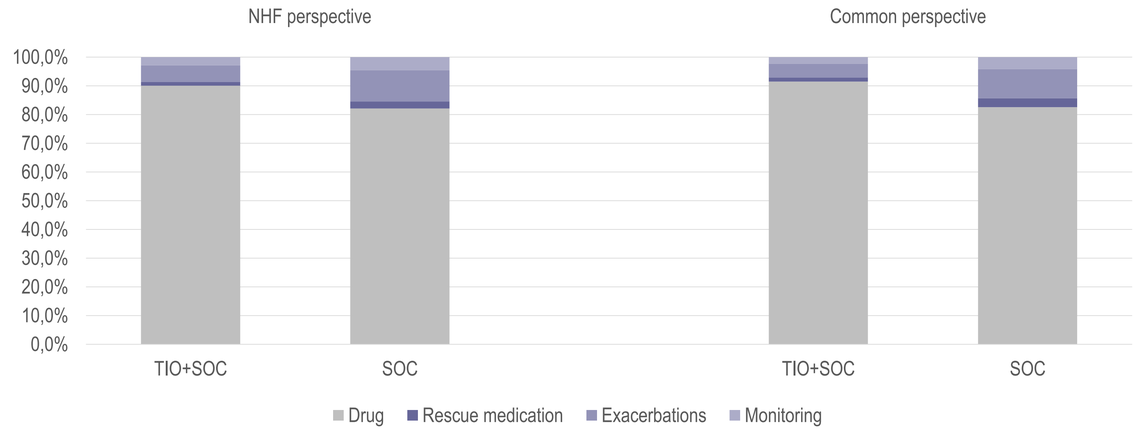
Table 2. *Model transition probabilities, SOC arm*

From \ To	Controlled asthma	Partly controlled asthma	Uncontrolled asthma	Non-severe exacerbation	Severe exacerbation - without hospitalisation	Severe exacerbation – with hospitalisation
"Early response phase"						
Controlled asthma	0.950	0.006	0.006	0.017	0.017	0.006
Partly controlled asthma	0.030	0.875	0.034	0.041	0.017	0.002
Uncontrolled asthma	0.015	0.023	0.927	0.025	0.009	0.001
Non-severe exacerbation	0.060	0.107	0.631	0.143	0.036	0.024
Severe exacerbation - without hospitalisation	0.083	0.063	0.292	0.042	0.500	0.021
Severe exacerbation – with hospitalisation	0.167	0.083	0.250	0.083	0.084	0.333
"Late response phase"						
Controlled asthma	0.943	0.015	0.008	0.023	0.010	0.001
Partly controlled asthma	0.031	0.901	0.027	0.030	0.009	0.001
Uncontrolled asthma	0.005	0.011	0.933	0.037	0.012	0.001
Non-severe exacerbation	0.123	0.107	0.551	0.208	0.009	0.002
Severe exacerbation - without hospitalisation	0.066	0.061	0.352	0.017	0.499	0.006
Severe exacerbation – with hospitalisation	0.118	0.029	0.294	0.088	0.030	0.441

Costs

Drug costs (tiotropium, ICS/LABAs), monitoring costs, rescue medication (salbutamol) costs and costs of exacerbations (requiring hospitalization and other) were considered. Costs were estimated in 2014.

Figure 2. *Distribution of costs*



Utilities

The health related utilities in the model were based on data from Primo-TinA-asthma trials [2] and from the published literature. Utility values associated with asthma control states were defined using the EQ-5D outcomes. For asthma exacerbations, EQ-5D utilities were obtained from a prospective study conducted in the UK at four specialist asthma centres (Lloyd 2007 [3]).

Table 3. *Utility values per health state*

Model parameter	Utility value	Reference
Controlled asthma state	0.937	Primo-TinA-asthma trials [2], Willson 2014 [1]
Partly controlled asthma state	0.907	Primo-TinA-asthma trials [2], Willson 2014 [1]
Uncontrolled asthma state	0.728	Primo-TinA-asthma trials [2], Willson 2014 [1]
Non-severe exacerbation state	0.649	Assumption, Willson 2014 [1]
Severe exacerbations without hospitalisation state	0.570	Lloyd 2007 [3], Willson 2014 [1]
Severe exacerbations with hospitalisation state	0.320	Lloyd 2007 [3], Willson 2014 [1]

Discounting: Within the base-case analyses, costs and health gains were discounted at 5% and 3.5%, respectively.

Compliance: It was assumed that compliance rate is 100%.

Uncertainty of results: Deterministic sensitivity analysis was performed to test the robustness of results in the presence of uncertainty.

RESULTS

Patients with severe persistent asthma benefit from the add-on treatment with tiotropium Respimat. The results of this cost-effectiveness analysis indicate that tiotropium as an add-on therapy to SOC in patients with severe asthma, results in improvement in health-related quality of life (higher QALYs) but at higher costs compared with SOC alone.

Tiotropium+SOC generated 13.616 quality adjusted life years in the life-time horizon, whereas SOC was associated with 13.367 QALY. The incremental cost-utility ratio (ICUR) of tiotropium+SOC vs SOC alone was estimated to be €16,137/QALY from the public payer's perspective. The ICUR from common (patient+NHF) perspective amounted to be €23,923/QALY. Both results were below the cost-effectiveness threshold accepted for Poland (€29,282/QALY).

Intervention	Costs (€)	QALYs	ICER (€/QALY)
The public payer's (National Health Fund - NHF) perspective			
TIO+SOC	10,460	13.616	-
SOC	6,432	13.367	-
Increments	4,028	0.2496	16,137
The common (patient and National Health Fund) perspective			
TIO+SOC	13,115	13.616	-
SOC	7,144	13.367	-
Increments	5,971	0.2496	23,923

1 € ≈ 4.08PLN

The deterministic sensitivity analysis showed robustness of the results.

CONCLUSIONS

Treatment of uncontrolled severe asthma with tiotropium delivered via Respimat added to high-dose inhaled corticosteroid and LABA is a cost-effective strategy in comparison to optimal SOC from both perspectives considered. The assessed technology is a response for existing unmet medical need in Poland.

References:

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