COST-UTILITY ANALYSIS OF ERDOSTEINE FOR THE PREVENTION OF EXACERBATIONS IN PATIENTS WITH COPD IN THE CZECH REPUBLIC

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Background

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory condition characterized by frequent exacerbations, which increase morbidity, mortality, and healthcare costs. Erdosteine, a mucolytic agent, when added to conventional COPD therapy, has demonstrated greater efficacy in reducing the rate and duration of COPD exacerbations, as well as disease severity, compared with conventional therapy alone.

Objective

The objective of this study was to evaluate the cost-utility of adding erdosteine to conventional therapy in patients with moderate to severe COPD who are at risk of exacerbations in the Czech Republic.
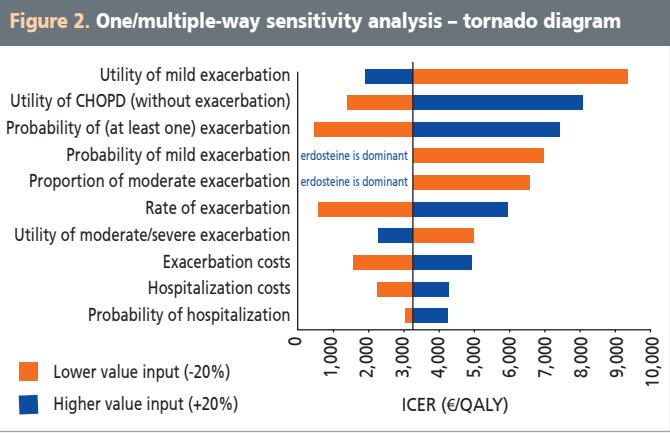
Methods

A one-year decision tree model was developed in TreeAge Pro 2025 to estimate quality-adjusted life years (QALYs) and treatment costs for erdosteine added to conventional COPD therapy compared with conventional therapy alone, from the healthcare payer's perspective. Given the one-year time horizon, no discounting was applied.

Model pathways were defined according to the presence and severity of exacerbations (mild, moderate, severe), and the occurrence of hospitalization associated with severe exacerbations. **Figure 1** illustrates the model structure.

Transition probabilities for exacerbation occurrence, distribution of exacerbation severity, and hospitalization following severe exacerbations were derived from the RESTORE trial[1-3]. Severity distribution was further informed by Wallace et al.[4]. **Table 1** summarizes the input parameters used for the derivation of transition probabilities.

Figure 1. Model structure

Table 1. Clinical data[1-4]

	Erdosteine	Placebo
Probability of (at least one) exacerbation in patients	57.7%	69.9%
Rate of exacerbation	0.91 per patient-year	1.13 per patient-year
Severity of exacerbation - Mild exacerbation - Moderate/severe exacerbation	62.6% 37.4% (moderate:severe 67.7%:32.3%)	
Probability of hospitalization due to severe exacerbation	80.1%	87.9%

Table 2. Utility of COPD with exacerbation[2,3,5]

		SGRQ total 0/6/12 months	EQ-5D utility 0/6/12 months & average
Erdosteine	Mild exacerbation	43.3/40.4/37.1	0.733/0.761/0.791 & **0.759**
	Moderate/severe exacerbation	49.1/47.4/48.2	0.674/0.692/0.684 & **0.683**
Placebo	Mild exacerbation	41.9/42.5/43.1	0.749/0.743/0.737 & **0.743**
	Moderate/severe exacerbation	49.5/45.5/49.7	0.669/0.712/0.667 & **0.683**

*Mapping Algorithm: EQ-5D utility = 0,9617 – 0,0013 SGRQ total – 0,0001 SGRQ total[2] + 0,0231 male

Utility values for COPD patients experiencing exacerbations, stratified by severity, were sourced from the RESTORE study[2,3], and derived using mapping algorithms between SGRQ and EQ-5D developed by Starkie et al.[5] (see **Table 2**). These utility values were further adjusted, where necessary, using utilities of the general population according to age and gender to ensure that exacerbation-related utilities did not exceed those of the general population (Ara et al.[6]). Utility values for COPD patients without exacerbations were estimated by applying age- and gender-specific values for the general population (Ara et al.[6]) and incorporating the disutility associated with COPD as reported by Sullivan et al.[6] (see **Table 3**).

Drug acquisition costs of erdosteine were derived from the SÚKL database of registered medicinal products[8] based on the recommended dosing regimen (i.e., 300 mg twice daily)[9]. Costs of exacerbations according to their severity were obtained from a Czech costing study (Skoupa et al.[10]) and inflated to current year prices using harmonized index of consumer

Table 3. Utility of COPD without exacerbation[6,7]

	EQ-5D utility
General population	0.819
COPD	0.792

*General population, EQ-5D utility = 0.9508566 + 0.0212126*male - 0.0002587*age - 0.0000332*age[2]

Table 4. Costs

	Costs
Drug acquisition costs, ERDOMED (erdosteine)	€236 per year
Exacerbation costs - Mild exacerbation - Moderate exacerbation - Severe exacerbation	€102 per year €583 per year €1,814 per year
Hospitalization costs, DRG 04-K06	€2,172 per hospitalization

prices (HICP)[11]. Costs of hospitalizations associated with severe exacerbations were sourced from a local DRG database (CZ-DRG version 7.0)[12]. An overview of all cost inputs is provided in **Table 4**.

To assess the robustness of the base-case deterministic results, extensive sensitivity analyses were conducted. These included probabilistic sensitivity analysis (PSA) with 1,000 iterations and a willingness-to-pay (WTP) threshold set at three times the GDP per capita in the Czech Republic (i.e. €47,873/QALY), as well as one-way and multi-way sensitivity analyses (OWSA/MWSA).

Results

Erdosteine reduced the annual exacerbation rate by 19.5% and decreased the proportion of patients hospitalized due to severe exacerbations by 7.8%.

Adding erdosteine to conventional COPD therapy resulted in an incremental QALY gain of 0.014 (0.757 vs. 0.743) at an additional cost of €46 (€586 vs. €540) compared to conventional COPD therapy alone over one year, yielding an incremental cost-effectiveness ratio (ICER) of €3,243 per QALY gained (see **Table 5**).

Treatment with add-on erdosteine resulted in the highest net monetary benefit (NMB) of €907,286, compared to €890,395 reached with standard therapy (see **Table 5**).

Sensitivity analyses (see **Figure 2** and **Figure 3**) confirmed that the mean probabilistic ICER, as well as ICERs from OWSA and MWSA, remained below the WTP threshold of €47,873 per QALY gained, confirming the robustness of the findings. The probability of erdosteine being cost-effective was nearly 60% at the selected WTP threshold.

Table 5. Base-case results of cost-utility analysis

	Erdosteine	Placebo	Difference
Total costs (€)	586	540	46
- Costs of erdosteine (€)	236	0	236
- Costs of mild exacerbation (€)	36	53	-17
- Costs of moderate exacerbation (€)	82	123	-41
- Costs of severe exacerbation (€)	122	182	-61
- Costs of hospitalization (€)	110	181	-71
QALY	0.757	0.743	0.014
- No exacerbation	0.335	0.241	0.094
- Mild exacerbation	0.274	0.325	-0.051
- Moderate exacerbation	0.100	0.120	-0.020
- Severe exacerbation	0.048	0.057	-0.009
ICER (€/QALY)			3,243
NMB (€)	907,286	890,395	NMB$_{erdosteine}$ > NMB$_{placebo}$

Conclusions

Adding erdosteine to conventional therapy in COPD patients at risk of exacerbations represents a cost-effective strategy from the Czech healthcare payer's perspective. This is primarily due to its ability to reduce both the exacerbation rate and severity, leading to improved patient quality of life and decreased healthcare resource utilization. The results are robust across sensitivity analyses.

These findings support the inclusion of erdosteine as an add-on therapy in routine COPD management, offering tangible clinical and economic benefits for patients and the healthcare system.

To our knowledge, this is the first cost-effectiveness analysis of erdosteine for preventing exacerbations in COPD patients, providing valuable evidence for decision-makers and clinicians in the Czech Republic.

Figure 2. One/multiple-way sensitivity analysis – tornado diagram

- Utility of mild exacerbation
- Utility of CHOPD (without exacerbation)
- Probability of (at least one) exacerbation
- Probability of mild exacerbation — erdosteine is dominant
- Proportion of moderate exacerbation — erdosteine is dominant
- Rate of exacerbation
- Utility of moderate/severe exacerbation
- Exacerbation costs
- Hospitalization costs
- Probability of hospitalization

ICER (€/QALY)

■ Lower value input (-20%)
■ Higher value input (+20%)

Figure 3. Probabilistic sensitivity analysis - cost-effectiveness scatter plot (left) and cost-effectiveness acceptability curve (right)

Incremental costs (€) / Incremental QALY

— WTP threshold
○ PSA iteration
○ Base-case deterministic ICER
○ Probabilistic ICER

Iterations Cost-Effective / WTP threshold (€/QALY)

— Erdosteine
— Placebo
— WTP threshold

* Distribution: gamma for costs, beta for probabilities and utilities, log-normal for rate

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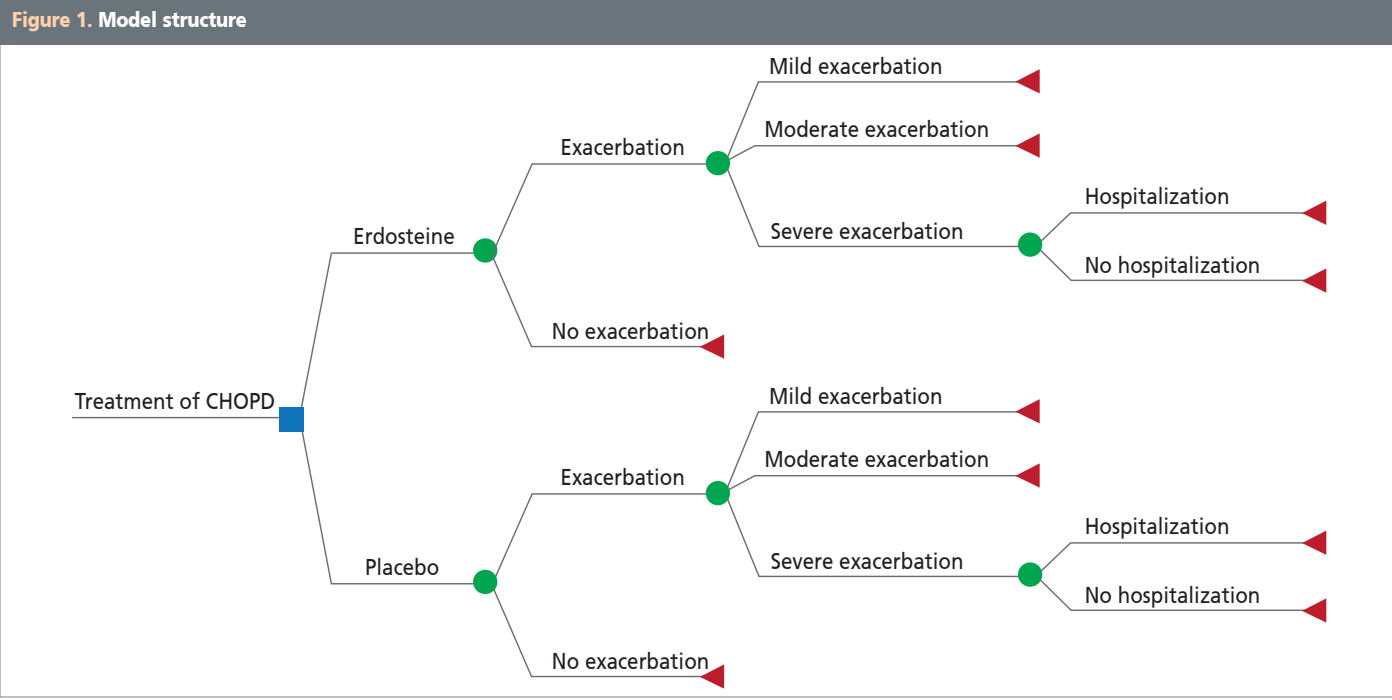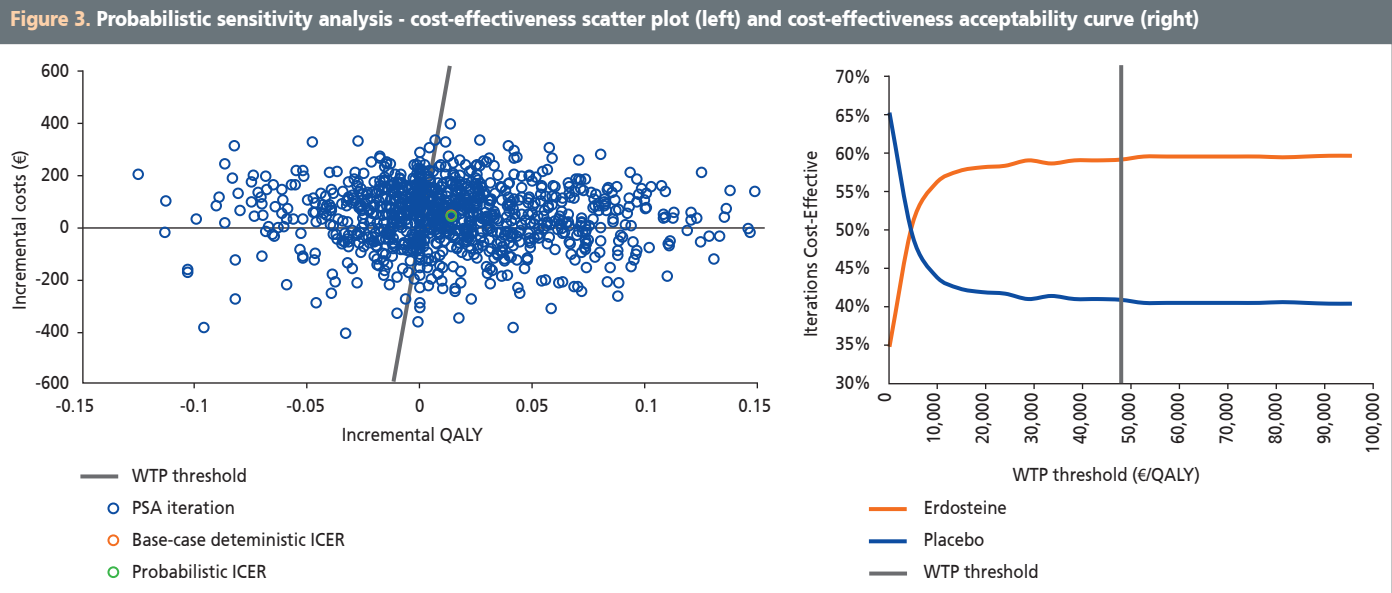
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