


# Cost-minimisation analysis of ravulizumab compared with eculizumab in patients with atypical Hemolytic Uremic Syndrome (aHUS) in the Netherlands


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### INTRODUCTION

- aHUS is a chronic rare disease, characterized by a dysregulated and overactive complement system. aHUS can affect both children and adults and has a lifelong risk of recurrence [1].
- This causes the formation of thrombi in small blood vessels, and can lead to the destruction of red blood cells, low platelets, and organ damage. In the acute state, 50% of patients with aHUS develop end-stage renal disease (ESRD), associated with kidney dialysis and transplants and with an overall mortality rate of 25% [2].
- Eculizumab, a complement C5 inhibitor, is currently the standard of care for patients with aHUS and has substantially improved patient prognosis. However, eculizumab requires biweekly infusions that can impose a large treatment burden on patients and caregivers [3].
- Ravulizumab, a long-acting complement C5 inhibitor, was approved for aHUS by the European Medicine Agency in 2021, in the treatment of patients with a body weight of ≥10 kg who are complement inhibitor treatment-naïve or have received eculizumab for ≥3 months and have evidence of response to eculizumab [4]. Ravulizumab was designed via targeted modification of eculizumab to leverage its clinical benefits and safety profile, while reducing dose frequency to every 4 to 8 weeks.



### OBJECTIVE

- To evaluate the economic impact of patients with aHUS switching from eculizumab to ravulizumab in the Netherlands from a societal perspective



### CONCLUSIONS

- Ravulizumab is cost-saving compared to eculizumab in both adult and paediatric patients with aHUS in the Netherlands, leading to a reduction in both lifetime medical and societal costs per patient.
- The cost-savings are mainly driven by a reduction in total treatment costs; however, ravulizumab also reduces the societal costs for patients and their families and, in the adult population, ravulizumab lowers the societal costs associated with productivity losses.

### METHODS

#### Model design

- A cost minimization Markov model was developed, assuming similar efficacy for eculizumab and ravulizumab (Figure 1).
  - Transition probabilities were based on the percentage of patients that discontinue treatment, the patients that relapse, and the mortality rate [5,6,7].
  - In the base case, it was assumed that all patients are in the “On Treatment” state and are chronically treated until death. The deterministic sensitivity analysis assessed the effect of early treatment discontinuation.
  - A lifetime horizon was used, with costs discounted at 4%.

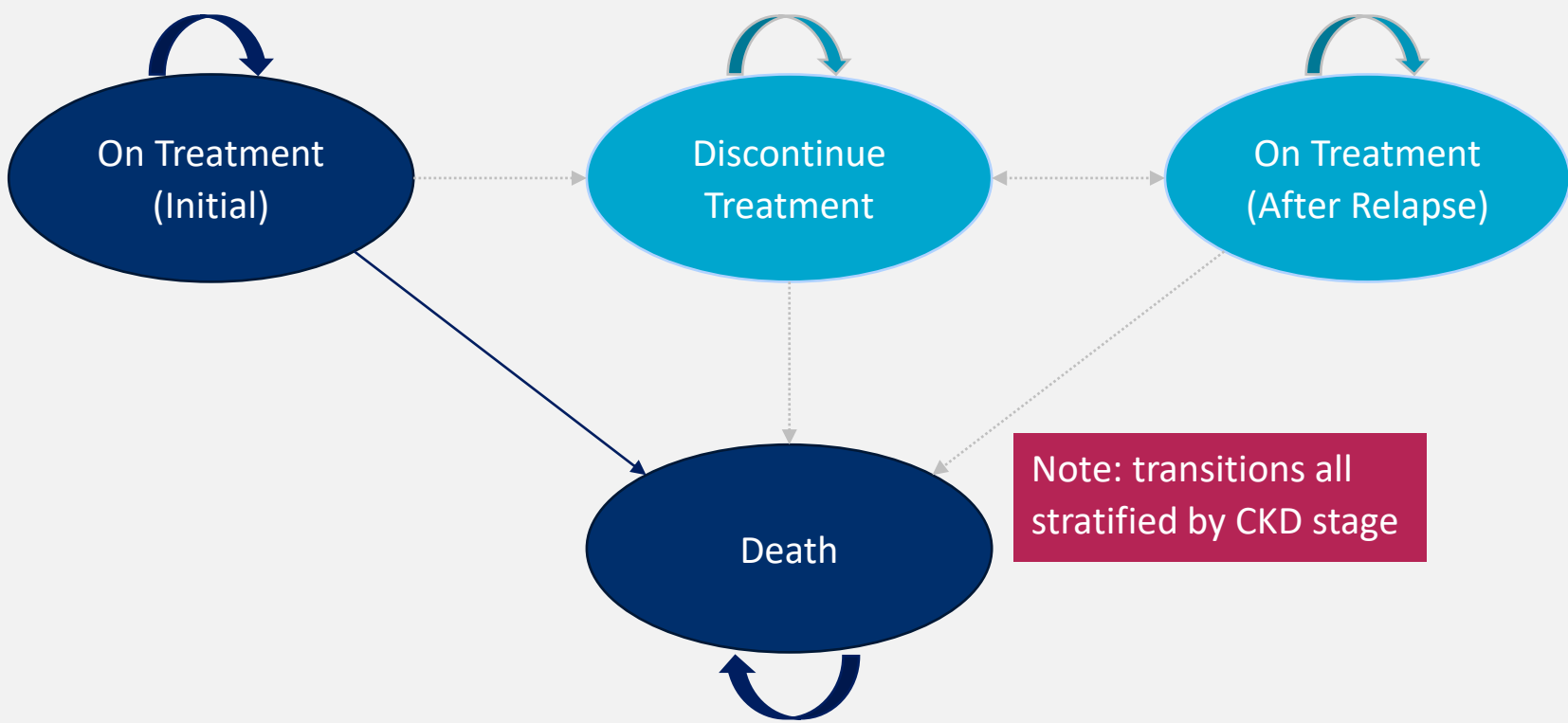


Figure 1. Model structure

#### Model inputs

- Patients were stratified in the following CKD stages:
  - Most adult patients were experiencing CKD 5 or ESRD (72.7%); otherwise 16.4% experienced CKD 4, 5.5% CKD3a/b and 5.5% CKD 0-2 [5]. The average age was 42 years.
  - Most paediatric patients experienced CKD 5 or ESRD (35.7%) and CKD 4 (42.9%); otherwise 7.1% experienced CKD 3a/b and 14.3% CKD 0-2 [6]. The average age was 6 years.
- The model included both medical costs and societal costs (Table 1).

Table 1. Key resource utilization and cost inputs in the model		
Resource	Input value	Reference
Medical Treatment	Drug acquisition costs Administration costs: Pharmacy preparation infusion; Infusion duration (€25.94 per hour)	Z-index list prices [8] Dutch costing manual [9]
Meningococcal vaccination costs at start of treatment)	€270.59	Z-index list prices [8]
Treatment discontinuation (monitoring costs, per 2-week cycle)	€5.29	Tariffs of creatinine and eGFR [10]
Costs of a relapse (per event, acute hospital event + management)	€1,563	Silver et al.; Cost of AKI [11]
Societal		
Travel (per infusion, monitoring, and relapse)	Costs per km: €0.19 Parking costs: €3.00 Distance to hospital: 14 km Distance to expertise centre: 147	Dutch costing manual [9];
Productivity losses (per infusion, monitoring, and relapse)	Cost per hour: based on wage and labour force for age distribution Time: ranging from 1.8-3.3 hours per infusion and 1 hour per monitoring and relapse	Dutch costing manual [9] CBS [12] Levy et al. [12]
Informal care (per infusion, monitoring, and relapse)	Cost per hour: €14.13 Time: ranging from 1.8-3.3 hours per infusion and 1 hour per monitoring and relapse	Dutch costing manual [9] CBS [13] Levy et al. [13]

#### Sensitivity analyses

- Scenario analyses were performed to asses the effect of:
  - A 1-year time horizon.
  - A 5-year time horizon.
- A deterministic sensitivity analysis was performed to establish the influence of the different parameters on the incremental costs when varied with a 95% confidence interval (CI). In the analysis the difference in costs of ravulizumab and eculizumab was calculated for the lower bound of the 95 CI and the upper bound of the 95% CI.

### RESULTS AND INTERPRETATION

#### Base case

- Ravulizumab was associated with lower lifetime per-patient costs than eculizumab in adult and paediatric patients with aHUS (Table 2).
- Most of the cost savings are related to the lower drug costs (Table 2), which reflect the economic impact of less frequent drug administrations required.
- Societal costs further exacerbated the difference in costs between ravulizumab and eculizumab.

Table 2. Base case of life-long treatment and medical costs per adult and paediatric patient			
Adult population			
	Ravulizumab	Eculizumab	Difference
Total costs	€6,583,061	€8,809,541	-€2,226,479 (-25%)
Treatment costs			
Drug costs	€6,563,522	€8,783,88	-€2,220,366
Administration costs	€7,639	€25,652	-€18,013
Societal costs			
Travel and informal care	€7,576	€29,910	-€22,334
Productivity losses	€4,325	€16,884	-€12,560
Paediatric population			
	Ravulizumab	Eculizumab	Difference
Total costs	€7,935,442	€10,934,538	-€2,459,095 (-24%)
Treatment costs			
Drug costs	€7,916,936	€10,363,220	-€2,446,284
Administration costs	€9,452	€31,318	-€21,866
Societal costs			
Travel and informal care	€9,054	€37,617	-€28,562


#### Sensitivity analyses

##### Scenario analysis

- Ravulizumab was cost-saving with both a 1-year and 5-year time horizon.

##### Deterministic sensitivity analysis

- In both adults and paediatric patients, the inputs with the greatest impact in driving costs were: the discount rate, the percentage of patients discounting with CKD stage >4 and the age at treatment start (Figure 2).



#### Figure 2. Tornado diagrams presenting the five most influential input parameters

**Note:** the Y-axis is intersecting the X-axis at the cost-difference in the base case  
The parameters were varied within their 95% CI to determine their influence on the cost difference between ravulizumab and eculizumab.  
Lower Parameter value = cost difference at low value of 95% CI; High parameter value = cost difference at high value of 95% CI

#### Disclosures

This study was funded by Alexion, AstraZeneca Rare Disease; funding support was provided to Asc Academics. A.J. Postma and S.W. Quist are employees of Asc Academics. Alexion AstraZeneca Rare Disease did not have any additional role in the study design, data collection and analysis.

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