A cost minimization and budget impact analysis of an eculizumab biosimilar, ABP 959, from the Spanish healthcare perspective

Vuvu F[1], Porter J[2], Sacrest Soy M[3], Arden M[4], Hirst A[4], Lashilola S[4]
[1]Amgen Inc, One Amgen Center Drive, Thousand Oaks, California, Unites States; [2]Amgen (Europe) GmbH, Suurstoffi 22, Rotkreuz, Zug, 6343, Switzerland; [3]Amgen (Spain), Placa Del Gas, Barcelona BRCL 08003, Spain;
[4]Adelphi Values PROVE, Bollington, Cheshire SK10 5JB, United Kingdom

ADELPHI VALUES | PROVE Expertise in Access and Value Evidence Outcomes

EE304

Introduction and objectives

- Paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS) are complement-mediated coagulation disorders associated with high morbidity and a quality-of-life detriment.[1]
- PNH is an acquired disease causing chronic red blood cell destruction, thromboembolism, and bone marrow failure, with an annual incidence of 5 to 6 cases per million people worldwide.[2-4] aHUS is a rare, frequently genetic, thrombotic microangiopathy characterized by microangiopathic hemolytic anemia, thrombocytopenia, and renal impairment, with an annual incidence of 0.23 to 1.9 cases per million people in Europe.[5]
- The current standard of care for PNH and aHUS is eculizumab, a humanized monoclonal antibody against C5, which gained marketing authorization in the European union (EU) in 2007.[6] Historically, the only other treatment option was ravulizumab, a non-inferior eculizumab-like C5 inhibitor with the advantage of a lower frequency of infusions which gained EU marketing authorization (EMA) in 2019.[7]
- However, in 2023, an eculizumab biosimilar, ABP 959, with demonstrated pharmacological and clinical similarity compared to the originator, received EMA approval.[8] This created an opportunity to reduce disease management costs based on a reduced drug acquisition cost compared to the incumbent treatments, and potentially yield significant budget savings for payers.
- Therefore, it is necessary to assess the economic impact of a reduced drug acquisition cost using ABP 959 given the clinically proven therapeutic equivalence with originator eculizumab and the assumed therapeutic equivalence with ravulizumab (based on the demonstrated non-inferiority of ravulizumab with originator eculizumab).[10] An assessment of the economic impact of ABP 959 is also useful given the lower administration cost of ravulizumab.[11]
- To this end, a cost-minimization analysis (CMA) and budget-impact analysis (BIA) were conducted; a CMA is appropriate for evaluating the relative affordability of biosimilars given the assumption of therapeutic equivalence, while a BIA can be used to assess the overall budget impact of adoption.[9]

Methods

- The analyses were conducted from the perspective of the Spanish health care system. Only drug acquisition and administration costs were considered; monitoring costs and adverse event costs were excluded due to the established similarity in the efficacy and safety profile between originator eculizumab, ravulizumab, and ABP 959.[10, 11]
- The CMA estimated the annual cost of treatment, per patient, for each treatment option. This informed the calculation of the annual cost saving per patient with ABP 959 compared with originator eculizumab and ravulizumab. The BIA estimated the budgetary impact, based on a five-year (2023-2027) time horizon, following the adoption of ABP 959 into the treatment mix. In the base case, the budget impact was based on the estimated total number of Spanish patients with PNH and aHUS receiving treatment over the 5-year period. In both analyses, results were first estimated by indication and by age-based subgroups, given differences in drug dosage (and thus administration costs) across these subgroups. The age-groups considered were patients <18 years old ('pediatric') and ≥18 years old ('adult'). Subsequently, subgroup results were combined to provide weighted average overall results.
- Epidemiological inputs (namely, estimates of the annual total general population in Spain, prevalence and incidence rates for each indication, and the proportion of the patient population treated in each indication) were sourced from published literature.[2, 12-15] In the scenario without ABP 959, it was assumed that originator eculizumab and ravulizumab had a 55% and 45% market share, respectively across all years, and in both indications (PNH and aHUS); in the scenario with ABP 959, it was assumed that market shares of ABP 959 would increase year on year to 57% and 55% in Year 5 for PNH and aHUS respectively (**Figure 1**).
- All drug acquisition costs were based on published list prices. The originator eculizumab and ravulizumab prices included in the model, across all years, were 4,450€ and 5,018€ respectively (**Table 1**).[16] The price for ABP 959 was 3,115€ in Year 1 based on its list price at launch (in 2023), and 2,220€ from Year 2 onwards (that is, Years 2-5 in the BIM).[16]
- The CMA distinguished between Year 1 and 'Subsequent years' given the presence of an induction phase in Year 1 (**Table 2**), which results in a higher administration cost in Year 1 compared to subsequent years. In Year 1, for each treatment, in each indication, in each age-group, an annual administration cost was calculated by multiplying the total number of infusions in the induction and maintenance phases (**Table 2**) by the unit cost of an intravenous infusion. As the annual number of infusions differed by bodyweight category (**Table 2**), a weighted average annual administration cost was calculated using the proportion of patients in each bodyweight category derived from a published source.[17] For administration costs in Year 2 onwards, only the infusion frequencies in the maintenance phase were used in the calculations. The unit cost of an intravenous infusion was estimated to be 157.65€ using reported 2014 costs inflated to 2024 prices according to the health component of the Spanish national consumer price index.[18]
- While the BIM reflected ABP 959 price changes over time, the CMA used a constant price both in Year 1 and in subsequent years. This is because the CMA is concerned with the annual per patient cost impact at a given ABP 959 price. Therefore, a base case analysis using the launch price of ABP 959 (3,115€) in Year 1 and subsequent years, and a scenario using the current price of ABP 959 (2,220€) in both treatment periods, were conducted.
- A one-way sensitivity analysis (OWSA) was conducted to test the robustness of the budget impact results, in which uncertain parameters were varied according to the 2.5th and 97.5th percentile. The values at these percentiles were calculated according to standard probability distributions assigned to each parameter, and an assumed standard error equal to 10% of the base case values.

Table 1. Price per vial of originator eculizumab, ravulizumab, and ABP 959

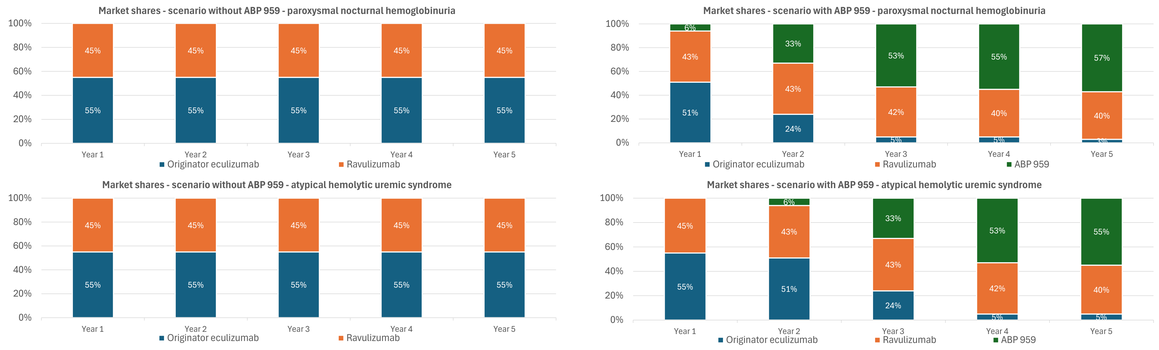
Product	List price: CMA base-case and BIM Year 1	List price: CMA scenario and BIM Years 2-5
Originator eculizumab	4,450€	4,450€
Ravulizumab	5,018€	5,018€
ABP 959	3,115€	2,200€

Table 2. Treatment dose and administration regimen for originator eculizumab, ravulizumab, and ABP 959

	Induction phase		Maintenance*	
	Dose	Frequency	Dose	Frequency
Originator eculizumab and ABP 959				
Adult patients and pediatric patients with bodyweight ≥ 40 kg†				
PNH	600	4 x QW	900	Q2W
aHUS	900	4 x QW	1,200	Q2W
Originator eculizumab and ABP 959				
Pediatric patients with bodyweight <40kg†				
PNH and aHUS				
30 to <40kg	600	2 x QW	900	Q2W
20 to <30kg	600	2 x QW	600	Q2W
10 to <20kg	600	1 x QW	300	Q2W
5 to <10kg	300	1 x QW	300	Q3W
Ravulizumab				
All patients‡				
PNH and aHUS				
≥100kg	3,000	1 x Q2W	3,600	Q8W
60 to <100kg	2,700	1 x Q2W	3,300	Q8W
40 to <60kg	2,400	1 x Q2W	3,000	Q8W
30 to <40kg	1,200	1 x Q2W	2,700	Q8W
20 to <30kg	900	1 x Q2W	2,100	Q8W
10 to <20kg	600	1 x Q2W	600	Q4W

* Maintenance starts from week 3
† Per EMA guidelines, pediatric PNH and aHUS patients with body weight ≥ 40 kg are treated with the adult dosing recommendations, respectively.[6,8]
‡ Per EMA guidelines, ravulizumab is indicated for the treatment of patients with a body weight of 10 kg or above.[7]
Abbreviations: PNH: Paroxysmal nocturnal hemoglobinuria; aHUS: atypical hemolytic uremic syndrome; QW: once weekly; Q2W: once every two weeks; Q3W: once every three weeks; Q4W: once every four weeks; Q8W: once every eight weeks; 1 x QW: one dose with the interval of one week; 2 x QW: two doses with the interval of one week.

Figure 1. Market share assumptions for paroxysmal nocturnal hemoglubinuria and atypical hemolytic uremic syndrome in the scenario with and without ABP 959



Results

- The CMA results are presented separately for Year 1 and subsequent years to account for the impact of induction dosing during Year 1 compared to the maintenance dosing in Year 2+ for all three treatments (**Table 3**). The results presented are weighted average results across indications. The indication-specific results are also weighted average results across age-groups: 92.5% and 7.5% of PNH patients were adult and pediatric patients respectively, while 40% and 60% of aHUS patients were adult and pediatric patients respectively, and 70.5% of all patients had PNH while the remaining 29.5% had aHUS.
- The CMA shows ABP 959 achieved an annual cost saving per patient between 102,168-110,885€ (approx. 30%) compared to originator eculizumab and between 33,426-119,588€ (12-32%) compared to ravulizumab, depending on the year and indication (**Table 4**). In the scenario using the current ABP 959 price (2,220€), ABP 959 achieved an annual cost saving between 172,194-186,885€ (approx. 50%) and 106,688-191,419€ (37-52%) compared to originator eculizumab and ravulizumab respectively (**Table 4**). This finding, of annual per-patient cost saving, was consistent across the pediatric and adult age-groups.
- Cost savings were driven by drug acquisition costs, both in the comparison with the originator and with ravulizumab. Although there was a small increase in drug administration costs compared to ravulizumab (between 2,782-3,282€ depending on age-group, year, and indication), savings in drug acquisition costs were substantially larger (between 21,291-126,122€ depending on age-group, year, and indication) **(Figure 2).**
- The BIA shows ABP 959 results in annual estimated budget savings of 1.8M€ (Year 1) and 53M€ (Year 5), with cumulative savings of 162.6M€ by Year 5 (**Table 5** and **Figure 3**).
- The OWSA showed that the parameter changes most strongly associated with larger budget savings included: a higher proportion of PNH patients receiving treatment, a higher PNH prevalence in adults, a higher uptake of ABP 959, a lower uptake of ravulizumab, and a higher PNH incidence in adults. (**Figure 4**).

Table 3. Cost (in €) per patient by year, indication, and treatment

	Base case analysis (using launch price of ABP 959)						Scenario analysis (using current price of ABP 959)					
	Year 1			Subsequent years			Year 1			Subsequent years		
	ABP 959	OE	RAVU	ABP 959	OE	RAVU	ABP 959	OE	RAVU	ABP 959	OE	RAVU
PNH	248,952	353,755	368,540	242,499	344,667	339,830	177,121	353,755	368,540	172,473	344,667	339,830
aHUS	263,030	373,915	307,203	253,471	360,362	286,898	187,030	373,915	307,203	180,209	360,362	286,898
WA	253,100	359,694	350,470	245,731	349,291	324,236	180,040	359,694	350,470	174,752	349,291	324,236

Abbreviations: aHUS: atypical hemolytic uremic syndrome; OE: Originator eculizumab; PNH: Paroxysmal nocturnal hemoglobinuria; RAVU: Ravulizumab; WA: Weighted average

Table 4. Absolute per patient cost saving (in €) compared to ABP 959, by year, indication, and treatment

	Base case analysis (using launch price of ABP 959)						Scenario analysis (using current price of ABP 959)					
	Year 1			Subsequent years			Year 1			Subsequent years		
	ABP 959	OE	RAVU	ABP 959	OE	RAVU	ABP 959	OE	RAVU	ABP 959	OE	RAVU
PNH	-	104,803	119,588	-	102,168	97,331	-	176,634	191,419	-	172,194	167,357
aHUS	-	110,885	44,173	-	106,890	33,426	-	186,885	120,173	-	180,152	106,688
WA	-	106,595	97,371	-	103,559	78,505	-	179,654	170,430	-	174,538	149,484

Abbreviations: aHUS: atypical hemolytic uremic syndrome; OE: Originator eculizumab; PNH: Paroxysmal nocturnal hemoglobinuria; RAVU: Ravulizumab; WA: Weighted average

Table 5. Budget impact (€) of introducing ABP 959 into the market across Year 1-5

	Year 1	Year 2	Year 3	Year 3	Year 5
Annual BI	- 1,818,124	- 19,648,367	- 39,708,189	- 48,474,128	- 53,011,617
% of costs	-1.26%	-12.76%	-24.19%	-27.80%	-28.71%
Cumulative BI	- 1,818,124	- 21,466,492	- 61,174,680	- 109,648,808	- 162,660,425
% of costs	-1.26%	-7.21%	-13.24%	-17.23%	-19.81%

Abbreviations: BI: Budget impact

Figure 2. Cost per patient, by year, treatment, and cost type

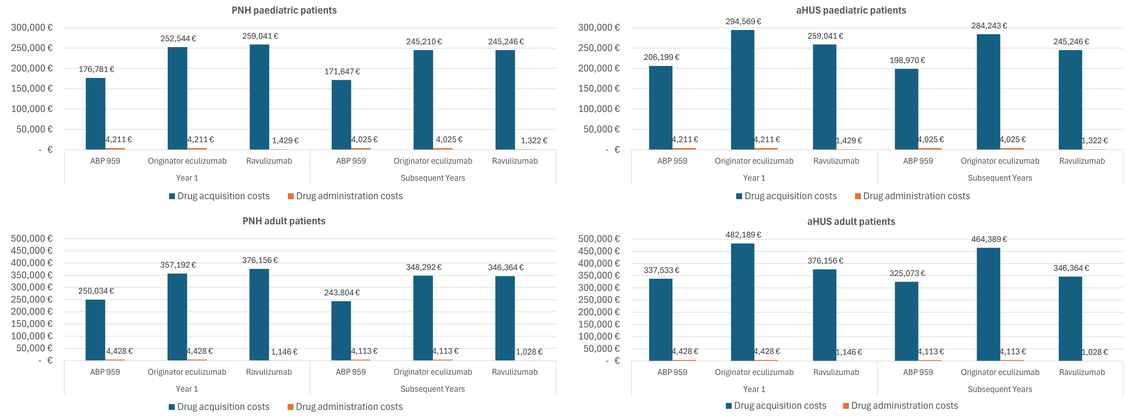


Figure 3. Annual and cumulative budget impact upon introduction of ABP 959

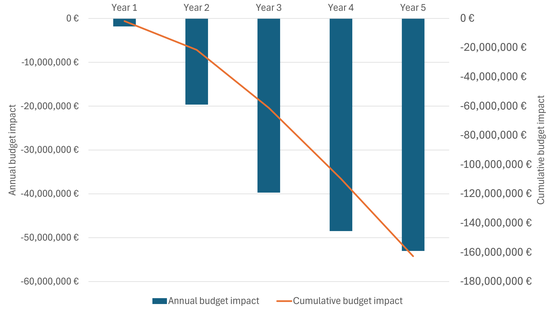
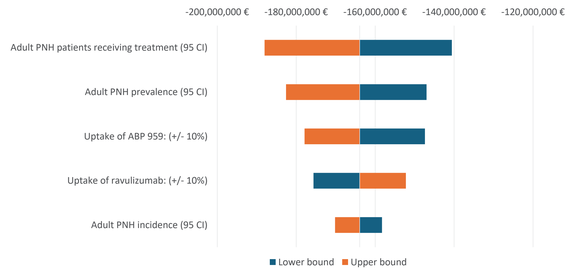


Figure 4. One-way sensitivity analysis results on the cumulative budget impact of ABP 959



Abbreviations: CI: confidence interval; PNH: paroxysmal nocturnal hemoglobinuria

Conclusion

- The CMA and BIA both demonstrated substantial estimated cost savings with ABP 959 compared with originator eculizumab and ravulizumab. The savings in drug acquisition costs offset the higher administration costs from more frequent administrations of ABP 959 compared with ravulizumab. The OWSA results indicate that increased uptake of ABP 959 result in increased budget savings. These results support the rapid adoption of ABP 959.

REFERENCES

1. Gavriilaki E, Brodsky RA. Complement-mediated coagulation disorders: paroxysmal nocturnal hemoglobinuria and atypical hemolytic uremic syndrome. Consultative Hemostasis and Thrombosis: Elsevier; 2019. p. 473-90; **2.** Bektas M, Copley-Merriman C, Khan S, Sarda SP, Shammo JM. Paroxysmal nocturnal hemoglobinuria: patient journey and burden of disease. Journal of managed care & specialty pharmacy. 2020;26(12-b Suppl):S8-S14; **3.** Farooq O, Saleem MW, Khan ZU, Hadi N. Paroxysmal Nocturnal Hemoglobinuria: A Diagnostic "Zero-Sum-Game". Cureus. 2020;12(12):e11956; **4.** Richards SJ, Painter D, Dickinson AJ, Griffin M, Munir T, Arnold L, et al. The incidence and prevalence of patients with paroxysmal nocturnal haemoglobinuria and aplastic anaemia PNH syndrome: A retrospective analysis of the UK's population-based haematological malignancy research network 2004-2018. Eur J Haematol. 2021;107(2):211-8 ; **5.** Yan K, Desai K, Gullapalli L, Druyts E, Balijepalli C. Epidemiology of Atypical Hemolytic Uremic Syndrome: A Systematic Literature Review. Clin Epidemiol. 2020;12:295-305; **6.** European Medicines Agency. Soliris : EPAR - Product information, summary of product characteristics (annex I). 2009; **7.** European Medicines Agency. Ultomiris : EPAR - Product information, summary of product characteristics (annex I). 2023; **8.** European Medicines Agency. Bekemv : EPAR - Product Information, summary of product characteristics (annex I). 2023; **9.** Simoens S, Jacobs I, Popovian R, Isakov L, Shane LG. Assessing the Value of Biosimilars: A Review of the Role of Budget Impact Analysis. Pharmacoeconomics. 2017;35(10):1047 62; **10.** Kulasekararaj A, Lanza F, Arvanitakis A, Langemeijer SM, Chonat S, Cao J, et al. Efficacy of Parallel and Crossover Analysis As Well As Pharmacokinetic Similarity Were Confirmed between ABP 959 and Eculizumab Reference Product in Patients with PNH. Blood. 2023;142:4092; **11.** Chow V, Pan J, Chien D, Mytych DT, Hanes V. A randomized, double-blind, single-dose, three-arm, parallel group study to determine pharmacokinetic similarity of ABP 959 and eculizumab (Soliris®) in healthy male subjects. European Journal of Haematology. 2020;105(1):66-74; **12.** Orphanet. Paroxysmal nocturnal hemoglobinuria 2024 [Available from: https://www.orpha.net/en/disease/detail/447] **13.** Orphanet. Atypical hemolytic uremic syndrome 2024 [Available from: https://www.orpha.net/en/disease/detail/2134] **14.** Instituto Nacional de Estadística. Resident population by date, sex and age (from 1971). 2024; **15.** IQVIA. IQVIA LAAD Data - analysis period Jan 2019-Jun 2020 [Data on file]. 2020; **16.** Consejo general de colegios farmaceuticos. Medicamentos, principios activos y laboratorios [Available from: https://www.farmaceuticos.com/botplus/buscador-botplus-lite/] **17.** Carrascosa Lezcano A, Fernández García JM, Fernández Ramos C, Ferrández Longás A, López-Siguero JP, Sánchez González E, et al. Spanish cross-sectional growth study 2008. Part II. Height, weight and body mass index values from birth to adulthood. An Pediatr (Barc). 2008;68(6):552-69; **18.** Instituto Nacional de Estadística. National indices: overall and by ECOICOP group. 2024.

DISCLOSURES & ACKNOWLEDGEMENTS

This study was funded by Amgen Inc., Thousand Oaks, CA and conducted in collaboration with Adelphi Values PROVE. Medical writing, editing, and design support were provided by Edward Oliver and Joe Handley of Adelphi Values PROVE.