

Costs of Treating Hereditary Angioedema (HAE) Attacks with C1 Inhibitors in Five Central and Eastern European Countries

Joanne B. Tutein Nolthenius¹, Raquel Figueiredo¹, Stuart Wood¹, John D. Whalen¹

¹Pharming Group N.V., Leiden, The Netherlands

BACKGROUND

Hereditary angioedema (HAE) is a rare genetic disease caused by the deficiency or dysfunction of C1 esterase inhibitor (C1-INH)¹, and characterized by recurring episodes of severe swelling, commonly affecting the skin, gastrointestinal tract, or upper airway (which can be life-threatening). Frequency and severity of attacks vary. Replacement C1-INH therapies provide effective relief; however, there is a lack of comparative data on economic outcomes. Our objective is to compare the differences in costs of treating acute HAE attacks with recombinant and human plasma-derived C1-INHs in five Central and Eastern European (CEE) countries.

Table 1. Acquisition costs of C1 inhibitors in 5 CEE countries.*

	Bulgaria	Czech Republic	Hungary	Poland	Romania
Ruconest® 2100 U powder and solvent for solution for injection	€744,02	€831,09	€738,02	€749,34	€737,60
Beriner® 500 IU / powder and solvent for solution for injection	€438,03	€518,06	€422,68	€447,15	€414,84
Beriner® 1500 IU powder and solvent for solution for injection	**	**	**	€1.341,45	**
Cinryze® 500 IU / powder and solvent for solution for injection	**	**	**	**	€1.140,24

*Prices derived from NAVLIN Price & Access Data database in local currency with the exchange rate of 22/6/2022.

**Product not available

METHODS

- Acquisition costs of recombinant and human plasma-derived C1-INH were collected from a price & access database² for Bulgaria, Czech Republic, Hungary, Poland and Romania (Table 1).
- Attack rate (26,9 per year³) and the mean number of doses required to control each attack were collected from published studies; data from randomized controlled studies (RCT) were analyzed separately from real-world and open-label studies (OLE) (Table 2).
- Cost per attack was estimated considering the distribution of patient weights⁴ (Table 3) and labelled dose regimens (Table 2).

Table 2. Dose regimen and re-dosing rates of C1-INH.

	Dose	RCT	Real-world/OLE
Ruconest®	50 U/kg ⁵	9,1% ⁸	0,2% ¹¹
Beriner®	20 U/kg ⁶	18,6% ⁹	1,1% ¹²
Cinryze®	1000 IU ⁷	65,7% ¹⁰	30,9% ¹³

Table 3. Weight distribution.

Weight category	Proportion of HAE patients
<25 kg	5%
25 – 42 kg	8%
42 – 50 kg	5%
50 – 75 kg	28%
75 – 84 kg	13%
84 – 100 kg	21%
100 – 125 kg	16%
125 – 150 kg	3%
150 – 175 kg	0%

Table 4. Average cost per attack in recombinant versus plasma-derived C1 Inhibitors including re-dosing rates.

	Bulgaria		Czech Republic		Hungary		Poland		Romania	
	RCT	OLE	RCT	OLE	RCT	OLE	RCT	OLE	RCT	OLE
Average cost per attack with Ruconest®	€1.520	€1.396	€1.698	€1.560	€1.508	€1.385	€1.531	€1.406	€1.507	€1.384
Average cost per attack with Beriner® 500 IU	€1.832	€1.562	€2.167	€1.847	€1.786	€1.507			€1.735	€1.479
Average cost per attack with Beriner® 1500 IU	**	**	**	**	**	**	€1.870	€1.594	**	**
Average cost per attack with Cinryze®	**	**	**	**	**	**	**	**	€1.889	€1.492
Average savings per patient per attack	€312	€166	€469	€288	€259	€122	€339	€188	€305	€101
Average savings per patient per year*	€8.391	€4.454	€12.610	€7.735	€6.993	€3.284	€9.124	€5.060	€8.206	€2.733

*Annualized costs based on mean attacks per year: 26,9¹⁸

**Product not available

RESULTS

- The proportion of patients requiring multiple doses to control an attack ranged from 9,1% to 65,7% in randomized studies and 0,2% to 30,9% in real-world studies.
- In general, recombinant C1-INH was less expensive than plasma-derived options, due to lower re-dosing rates.
- In the analysis using randomized studies, average savings per patient when using recombinant C1-INH were €312 per attack (€8.391 per year) in Bulgaria, €469 (€12.610) in Czech Republic, €259 (€6.993) in Hungary, €339 (€9.124) in Poland, and €305 (€8.206) in Romania.
- In the analysis using real-world studies, average savings per patient were €166 per attack (€4.454 per year) in Bulgaria, €288 (€7.735) in Czech Republic, €122 (€3.284) in Hungary, €188 (€5.060) in Poland, and €101 (€2.733) in Romania.

CONCLUSIONS

- Based on published studies and drug prices, treatment with recombinant C1-INH may require fewer repeat doses to control an HAE attack and provide savings in CEE countries, compared to plasma-derived products.
- In addition to the economic impact of re-dosing, future analyses should consider the humanistic impact of rapid control of attacks.

REFERENCES

- Zuraw BL, et al. Hereditary angioedema. N Engl J Med. 2008;359:1027–36.
- Navlin Price & Access database by Eversana.
- Lumry WR. Hereditary angioedema: the economics of treatment of an orphan disease. Front Med (Lausanne). 2018;5:22.
- Reshef A. Recombinant human C1 esterase inhibitor treatment for hereditary angioedema attacks in children. Pediatr Allergy Immunol. 2019 Aug;30(5):562–568.
- Ruconest (conestat alfa) Summary of Product Characteristics. 2020. Leiden, the Netherlands: Pharming Group NV.
- Beriner (plasma-derived C1-INH) Summary of Product Characteristics. 2021. CSL Behring.
- Cinryze (plasma-derived C1-INH) Summary of Product Characteristics. Shire. 2016.
- Riedl MA, et al. Recombinant human C1-esterase inhibitor relieves symptoms of hereditary angioedema attacks: phase 3, randomized, placebo-controlled trial. Ann Allergy Asthma Immunol. 2014;112(2):163–169.
- Craig TJ, et al. Efficacy of human C1 esterase inhibitor concentrate compared with placebo in acute hereditary angioedema attacks. J Allergy Clin Immunol. 2009 Oct;124(4):803–8.
- Zuraw BL, et al. Nanofiltered C1 inhibitor concentrate for treatment of hereditary angioedema. N Engl J Med. 2010;363:513–522.
- Valerleva A, et al. Recombinant human C1 esterase inhibitor for hereditary angioedema attacks: A European registry. World Allergy Organ J. 2021; 14(4): 100535.
- Craig TJ, et al. C1 esterase inhibitor concentrate in 1085 hereditary angioedema attacks – final results of the I.M.P.A.C.T.2 study. Allergy. 2011; 66: 1604–11.
- Riedl MA, et al. Nanofiltered C1 esterase inhibitor (human) for the treatment of acute attacks of hereditary angioedema: an open-label trial. Ann Allergy Asthma Immunol. Jan 2012;108(1):49–53.