Original Research

# Cost-effectiveness of treatment schemes in wet age-related macular degeneration in Colombia

## Costo-efectividad de esquemas de tratamiento de la degeneración macular asociada con la edad húmeda en Colombia

Sahir Camilo Basto Fajardo[1] https://orcid.org/0000-0002-7036-610X
Ariel Emilio Cortés Martínez[1] https://orcid.org/0000-0002-1169-9086
Carmen Elisa Becerra Huertas[2*] https://orcid.org/0000-0002-4325-652X

[1]Pontificia Universidad Javeriana, Escuela de Economía y Negocio. Bogotá, Colombia.
[2]Universidad Colegio Mayor de Cundinamarca, Escuela Ciencias de Salud. Bogotá, Colombia.

*Author correspondence: carmen.becerra@unicolmayor.edu.coge

**ABSTRACT**

**Introduction:** Comparison of costs in intravitreal treatment regimen for Wet Age-Related Macular Degeneration (Wet-AMD) in fixed-treat and extend regimens for Ranibizumab and Aflibercept.

**Objective**: Cost-effectiveness analysis according to the frequencies used and recommended without loss of vision obtained in two years of treatment.

**Methods:** Cost effectiveness analysis in administrative reports (SISMED base of Colombia) third quarter of 2020 - 2021; Sensitivity analysis with the new presentation of Aflibercept pre-filled syringe versus the pre-filled presentation of Ranibizumab. Values data correspond to billable dispensing units; the effectiveness is the frequency of application of the drugs in which the scientific literature certifies the non-loss of the gain of letters acquired by the patients.

**Results:** The fixed dose model Aflibercept therapy for Wet-AMD presents a greater gain than Ranibizumab in comparative effectiveness of 18.0%, influenced by the frequency, the percentage of cost variation 22.1% in favor of Aflibercept. The cost-effectiveness model to treat - extend shows a gain in comparative effectiveness of 40.4% and the variation in cost of 11.2% for Aflibercept. The sensitivity model in two years of treatment shows; fixed-dose regimen Ranbizumab U$ 8 965.1 and Aflibercept U$ 5,661.3. In the treat - extend model, in the same period, it reports Ranibizumab U$ 6 884.4 and Aflibercept U$ 5 035.6.

**Conclusion:** Both Ranibizumab and Aflibercept are indicated for the treatment of Wet-AMD, with reported vision gain, the frequency in the fixed dose scheme and treat - extend are lower in Aflibercept. Greater cost effectiveness was evidenced in Aflibercept, influenced by the number of applications in the two comparative models. The sensitivity study for the new presentation of Aflibercept generates lower costs in two years of treatment, however, more data is required in administrative bases to infer the cost containment in the treatment compared to Ranibizumab.

**Keywords:** cost-effectiveness treatment Aflibercept *versus* Ranibizumab; Macular degeneration associated with the humid age.

## RESUMEN

**Introducción:** La degeneración macular asociada con la edad húmeda ocurre cuando nuevos vasos sanguíneos anormales se desarrollan debajo de la retina (proceso de neovascularización coroidea) y precisa de tratamiento de por vida, por lo que la comparación de costos en el régimen de tratamiento intravítreo fijo y de extensión para Ranibizumab y Aflibercept se hace necesario

**Objetivo:** Analizar costo-efectividad según frecuencias utilizadas y recomendadas sin pérdida de visión obtenida en dos años de tratamiento.

**Métodos:** Se realizó análisis de costo efectividad en reportes administrativos Sistema de Información de Precios de Medicamentos (SISMED base de Colombia) 2020 – 2021 (tercer trimestre), análisis de sensibilidad con nueva presentación de Aflibercept jeringa prellenada *versus* presentación prellenada de Ranibizumab. Los datos de valores corresponden a unidades facturables de dispensación, efectividad según frecuencia de aplicación de

medicamentos en las cuales la literatura científica certifica la no pérdida de ganancia de letras adquiridas por los pacientes.

**Resultados:** El modelo de dosis fija Aflibercept terapia presenta mayor ganancia que Ranibizumab en eficacia comparativa (18,0 %), influenciado por frecuencia y porcentaje de variación de costos (22,1 %) a favor de Aflibercept. El modelo de coste-efectividad a tratar-ampliar mostró ganancia en eficacia comparativa (40,4 %) y variación en costo (11,2 %) para Aflibercept. El modelo de sensibilidad en dos años de tratamiento mostró; régimen de dosis fija Ranbizumab U$ 8 965,1 y Aflibercept U$ 5 661,3. En el modelo tratar-extender, en igual período, reporta Ranibizumab U$ 6,884,4 y Aflibercept U$ 5 035,6.

**Conclusiones:** Ambos medicamentos están indicados para tratar la enfermedad con ganancia de visión reportada, frecuencia en esquema de dosis fija y tratamiento extendido menores en Aflibercept. Se evidenció mayor rentabilidad en Aflibercept, influida por el número de aplicaciones en ambos modelos comparativos. El estudio de sensibilidad para la nueva presentación de Aflibercept generó menores costos en dos años de tratamiento, sin embargo, se requieren más datos en bases administrativas para inferir contención de costos en tratamiento comparado con Ranibizumab.

**Palabras clave:** costo-efectividad tratamiento Aflibercept *versus* Ranibizumab; degeneración macular asociada con la edad húmeda.

Received: 11/07/2023

Accepted: 27/10/2023

## Introduction

Wet Age-Related Macular Degeneration (Wet-AMD) is the main cause of vision loss in people over 55 years.[1] Currently in Colombia there are anti-angiogenic drugs that inhibit the vascular endothelial growth factor A (anti-FEVG) which limits neo-vascularization and prevents vision loss.[2]

Two clinical types of Wet-AMD: dry or atrophic and the wet one related to the progression of the disease: exudative changes. Wet-AMD has two variants: classic has neovascularization due to angiographic studies, and hidden variant where there are no neovascularizing changes with ongoing disease progression.[3,4]

Current treatment for Wet-AMD is mainly the application of intravitreal injections of Vascular Endothelial Growth Factor (VEGF) inhibitors, other treatment alternatives: photocoagulation and photodynamic therapy.[5] Currently the inhibitors (VEGF) used in Colombia for the treatment of Wet-AMD are: Ranibizumab (Lucentis ®, Novartis) and Aflibercept (EyLea ®, Bayer Pharmaceuticals).

Ranbizumab is an immunoglobulin G1 monoclonal antibody fragment with a molecular weight of 48 Kd, it allows diffusion in the retina and choroids, the recommendation for classic treatment is 0.5 mgr monthly intravitreal injection.[5,6]. Aflibercept is a recombinant VEGFR-1 and 2 fusion protein with a molecular weight of 97 Kd.[7]

Conventional application of treatments uses the technique: intravitreal; the number of applications changes according to the established protocols, in recent years the number of doses applied has decreased with similar results of efficacy and effectiveness, scheme: treat-extend, patients with dose treatments fixes-maintained recovery if they changed to treat-extend schemes, improves therapeutic adherence.[8]

Concentration of Ranibizumab and Afliberpcet are different, the comparisons within the reported literature are not direct, the costs and commercial presentations have changed in recent years, the objective of this study is to determine the cost effectiveness of fixed dose and extension schemes available in Colombia for Wet-AMD.

Cost-effectiveness analysis is a form of economic appraisal useful. Both Ranibizumab and Aflibercept are indicated for the treatment of Wet-AMD, with reported vision gain, the frequency in the fixed dose scheme and treat - extend are lower in Aflibercept. Greater cost effectiveness was evidenced in Aflibercept, influenced by the number of applications in the two comparative models. The sensitivity study for the new presentation of Aflibercept generates lower costs in two years of treatment, however, more data is required in administrative bases to infer the cost containment in the treatment compared to Ranibizumab

This study analysis projects, from the Colombian health care system payer`s perspective and for a two-year period beginning 2021, the costs of T&E anti-VEGF therapy with both medications in the treatment of Wet-AMD.

## Methods

Cost-effectiveness study includes a literature review in the PubMed database comparing intravitreal treatment regimens and their costs for Ranivizumab and Aflibercept: fixed doses and treat-extend for Wet-AMD in adult patients.

The inclusion criteria: meta-analysis and systematic reviews published in the last ten years and the words used for the search were: *age-related macular degeneration, intravitreal anti-vascular endothelial growth factor therapy factor, cost effectiveness*.

The search determined forty articles, of which seven were selected that complied with the report of intravitreal injections in the fixed regimens and treat and extend (table 1)

**Table 1 -** Systematic Review

| Author | Scheme of intravitreal injections |
|---|---|
| Ba *et al*, 2015[9] | The Aflibercept scheme every 2 months required fewer injections than Ranbizumab which was applied monthly. The efficacy of both treatments is similar. Patients with Aflibercept every 8 weeks achieved similar visual results to the Ranibizumab group with every 4 weeks scheme with a mean of five fewer injections over 96 weeks. |
| (Sarwar, *et al*, 2016)[10] | Monthly ranibizumab injections are used for fixed treatment in patients with WET-AMD. In the first year of treatment, doses were administered every four weeks to eight weeks. Afliblibercept presents treatment schedules with longer intervals between each application. |
| (Regnier, et al. 2016)[11] | Indirect comparison of the concentrations of Aflibercept 2 mg every 8 weeks and Ranibizumab 0.5 mg. No statistically significant differences were found in mean gain in baseline best-corrected visual acuity from baseline at month 12 between Ranibizumab and Aflibercept. |
| (Zhang, et al., 2017)[12] | The number of aflibercept injections during the first year of treatment ranged from 4.3 to 5.9, and ranibizumab required 4.5 to 8.37 injections. Aflibercept required fewer injections than Ranibizumab. |
| (Empeslidis, et al., 2019)[13] | Some studies have shown a significant reduction in the number of injections after a therapeutic switch to Aflibercept. |

| | |
|---|---|
| (Plyukhova, et al., 2020)[14] | The number of injections required to achieve clinical effects was less for Aflibercept. Aflibercept injections were about five fewer than Ranibizumab at the end of two years. Some Endophthalmitis is the most reported adverse event in regimens with more doses of intravitreal injections. |
| (Ohji, et al., 2020)[15] | At 2 years of treatment with Aflibercept Treat and Extend scheme was on average six injections less than Ranibizumab in the same scheme. The mean number of injections received by patients treated with Aflibercept fixed versus treat-extend at week 96 was 11.2 and 10.4, respectively. |

The costs were taken from the *Sistema de Información de Precios de Medicamentos (SISMED-Colombia)*, prices 2020 and 2021 of reported monetary values, commercial presentation, dispensing unit, minimum concentration unit, unit per primary packaging; other value of the new pre-filled presentations Aflibercept in 2021.[16]
Two models are presented:

1. Cost effectiveness: fixed dose: Ranibizumab uses 21.3 doses and Aflibercept 11.7 doses. Treat-extend Ranibizumab uses 16.6 doses and Aflibercept 10.4.
2. Sensitivity: fixed dose vs trying to extend with a new pre-filled presentation.

In 2020, the commercial presentation of Aflibercept in Colombia was in a 11.1 mg vial and Ranibizumab was marketed as a 10 mg/ml injectable solution, the data are from the third quarter in the SISMED base for both drugs, with a weighted average price. minimum and the dollar reference in the third quarter 2020 TRM ($ 3.730.5) and third quarter 2021 TRM ($ 3.844.3).
The year 2021 there is a new presentation of Aflibercept, it changes the filling volume from 278 µL to 177 µL and concentration from 11.1 mg to 7.1 mg and an estimated value between $ 474.6 To adjust year 2 of treatment the reported monetary values are adjusted with expected inflation 2021.
Costs of perioperative medications (topical antibiotics, analgesics) were not included. The frequency and costs of medical examinations and tests were identical for both treatment groups. Costs for the treatment of adverse events were not considered. A 5.0% discount rate

for costs and outcomes was applied. We used Consolidated Health Economic Evaluation Reporting Standards (CHEERS).[17]

## Results

The treatment lengthening schemes endorsed for the drug Aflibercept, in pivotal studies were up to week 52,[18] however, the treatment between the five and seven subsequent doses has shown no loss of the gain in letters, with a reduced number of patients.

The fixed scheme Ranibizumab established 21.3 applications distributed in the first year 11.2 and the second year 10.1. Aflibercept, it established 11.7 applications distributed in the first year 7.5 and 4.2 in the second year.

The treat and extend scheme Ranibizumab established 16.6 applications distributed in the first year 9.1 and the second year 7.5.

For Aflibercept it established 10.4 applications distributed in the first year 6.9 and in the second year 3.5.[19]

The SISMED base values for Aflibercept was 43.683 units invoiced, only accepting values greater than 100 dollars were reported 39.451 equivalents to 90.3%. Ranibizumab 43.108 units billed with a similar restriction of 100 dollars was reported: 41.709 equivalents to 96.8%.

Percentiles analysis 25, 50 and 75 the values with less variation to perform the analysis and attenuate other factors that may influence the final value, the dispensing unit had a variation of 29,0% between the two drugs, it was obtained:

- Aflibercept 18,684 records, grouped in 122 billing unit reports,
- Ranibizumab 19,983 records, grouped in 126 billing unit reports.

Reported minimum unit prices were analyzed, finding that the 25th percentile of aflibercept was close to the upper limit of mild extreme cases of Ranibizumab and the smallest score of the variable for Aflibercept was in the range Q1 to Q3 of Ranibizumab.

In year 1 the loading doses were similar for both technologies: 1 monthly dose in the first three months. In model 1, values corresponding the percentile 25th are included, the

effectiveness is the frequency of applications without the gain of letters decreasing in the second year of application (table 2).

**Table 2 -** Fixed treatment scheme model 1

| Fixed treatment scheme model 1 | | | | | Percentil 25 |
|---|---|---|---|---|---|
| **Fixed treatment scheme** | **Ranibizumab** | **Year 1** | **Initial dose (3 months)** | **3** | **$ 1 160,93** |
| | | | Follow-up treatment | 8,2 | $ 3 173,21 |
| | | Year 2 | Follow-up treatment | 10,1 | $ 3 908,47 |
| | | Total, Ranibizumab | | 21,3 | $ 8 242,61 |
| | Aflibercept | Year 1 | Initial dose (3 months) | 3 | $ 1 646,37 |
| | | | Follow-up treatment | 4,5 | $ 2 469,55 |
| | | Year 2 | Follow-up treatment | 4,2 | $ 2 304,91 |
| | | Total, Aflibercept | | 11,7 | $ 420,83 |
| Treat and extend | Ranibizumab | Year 1 | Initial dose (3 months) | 3 | $ 1 160,93 |
| | | | Follow-up treatment | 6,1 | $ 2 360,56 |
| | | Year 2 | Follow-up treatment | 7,5 | $ 2 902,33 |
| | | Total, Ranibizumab | | 16,6 | $ 6 423,82 |
| | Aflibercept | Year 1 | Initial dose (3 months) | 3 | $ 1 646,37 |
| | | | Follow-up treatment | 3,9 | $ 2 140,28 |
| | | Year 2 | Follow-up treatment | 3,5 | $ 1 920,76 |
| | | Total, Aflibercept | | 10,4 | $ 5 707,41 |

The second model used the median in Ranibizumab of all the values reported in the administrative base, the value for Aflibercept corresponds to the one reported in the regulatory price framework for Colombia without any historical record.

The application rate values are maintained for both fixed treatment and treat-extend drugs (table 3).

**Table 3 -** Fixed treatment scheme with median model 2

| Fixed treatment scheme with median model 2 | | | | | Median |
|---|---|---|---|---|---|
| Fixed treatment scheme | Ranibizumab | Year 1 | Initial dose (3 months) | 3 | $ 1 262,68 |
| | | | Follow-up treatment | 8,2 | $ 3 451,33 |
| | | Year 2 | Follow-up treatment | 10,1 | $ 4 251,03 |
| | | Total, Ranibizumab | | 21,3 | $ 8 965,05 |
| | Aflibercept | Year 1 | Initial dose (3 months) | 3 | $ 1 467,25 |
| | | | Follow-up treatment | 4,5 | $ 2 200,87 |
| | | Year 2 | Follow-up treatment | 4,2 | $ 1 993,16 |
| | | Total, Aflibercept | | 11,7 | $ 5 661,27 |
| Treat and extend | Ranibizumab | Year 1 | Initial dose (3 months) | 3 | $ 1 262,68 |
| | | | Follow-up treatment | 6,1 | $ 2 567,45 |
| | | Year 2 | Follow-up treatment | 7,5 | $ 3 054,25 |
| | | Total, Ranibizumab | | 16,6 | $ 6 884,38 |
| | Aflibercept | Year 1 | Initial dose (3 months) | 3 | $ 1 467,25 |
| | | | Follow-up treatment | 3,9 | $ 1 907,42 |
| | | Year 2 | Follow-up treatment | 3,5 | $ 1 660,96 |
| | | Total, Aflibercept | | 10,4 | $ 5 035,63 |

Cost effectiveness: The effectiveness was defined as that in which there was no significant loss of letters compared to the number of doses used in a period of 2 years, to generate the comparison the lowest value reported as 100.0% of effectiveness was considered, inferring the best adherence to the treatment reported in the literature, in this study greater applications decreased effectiveness (table 4).

**Table 4 -** Cost effectiveness analysis

| Application dose | | | | Percentil 25 | | |
|---|---|---|---|---|---|---|
| - | - | Application | Equivalent effectiveness | Percentil 25 dispensing unit | Average cost effectiveness ratio | - |
| Fixed treatment scheme | Ranibizumab | 21,3 | 82,1 | $ 8 242,61 | 100,5 | Dominated |
| | Aflibercept | 11,7 | 100 | $ 6 420,83 | 64,2 | - |
| Treat and extend | Ranibizumab | 16,6 | 59,6 | $ 6 423,82 | 107,8 | Dominated |
| | Aflibercept | 10,4 | 100 | $ .707,41 | 57,1 | - |

In the fixed scheme, the difference in effectiveness between treatments was 18.0% and, in the treat-extend it was 40.4%, the average cost-effectiveness ratio shows a lower cost when treating with Aflibercept for the treatment in the two schemes evaluated. which implies that the dominated variable is Ranibizumab.

Sensitivity analysis: The entry into the market of pre-filled doses has decreased the concentration of the drug, however, in the literature the same number of doses is expressed in the treatment period, then the value decreases due to the concentration.

The reported value of Aflibercept does not have data in the 2021 period, a sensitivity study is carried out, and the median parameter as central tendency is used for its analysis to make the comparison between the two technologies (table 5).

**Table 5 -** Sensivity analysis.

| - | - | Application dose | | | Median | | |
|---|---|---|---|---|---|---|---|
| | | Application | % | Equivalent effectiveness | Value | Average cost effectiveness ratio | - |
| Fixed treatment scheme | Ranibizumab | 21,3 | 182,051282 | 82,0512821 | $ 8 965,05 | 109,3 | Dominated |
| | Aflibercept | 11,7 | 100 | 100 | $ 5 661,27 | 56,6 | |
| Treat and extend | Ranibizumab | 16,6 | 159,615385 | 59,6153846 | $ 6 884,38 | 115,5 | Dominated |
| | Aflibercept | 10,4 | 100 | 100 | $ 5 035,63 | 50,4 | |

There is evidence of a slight increase in the value of ranibizumab technology for the classic treatment of 8.8% and for the treat-and-extend scheme of 7.2%, considering that this technology presents higher atypical data. For its part, Aflibercept shows a single value without billable units; the initial estimated value has a reduction of 11.8% in the fixed treatment and 13.3% in the treat and extend scheme.

## Discussion

The values reported in the administrative base show a higher value per unit for Aflibercept compared to Ranibizumab, the available literature has alternative protocols for intravitreal treatment (treat -extend) in which Aflibercept shows maintenance of clinical results with a significant decrease in costs.

The data suggest that the lower number of doses applied can generate greater adherence to treatment, consequently with fewer risks of adverse events and complications, finding cost reductions up to 33.0 % in the sequence between week 52 and 96.[20]

The two technologies analyzed show reductions in the value for the two years of the study, finding more atypical data reported in Ranibizumab, which would influence the median, being lower for this technology compared to Aflibercept in the values of minimum prices reported in the units. dispensing.

The dose adjustments reported in presentations for the two drugs have gone from vial to a pre-filled syringe, the main changes are in the concentration, in the case of Aflibercept it goes from 11.1 mgr. to 7.1 and an estimated reduction in its value. For Ranibizumab, the established value corresponds to the pre-filled presentation of 1.7 mgr., the values consulted for Colombia are regulated by the Ministry of Health.

The comparison between these two technologies is still incipient since the data provided for the first model compare values of presentations with different concentrations: Ranibizumab the report of value per milligram corresponds to 1.7 mg / 0.165 mL and for Aflibercept the report of the vial of 2mgr/ 0.05ml. In the second model, the Aflibercept value is adjusted with an estimated single value by performing a sensitivity analysis.

Both technologies show differences between their molecular structures, Ranibizumab being a Fab fragment and Aflibercept being a VEFGR ½-Fc protein fusion, which implies a higher molecular weight.(11)

Both technologies at the established frequencies manage to control and improve the quality of life of users who have a diagnosis of Wet-AMD, for the fixed and treat-extend schemes, a decrease in the frequency is evidenced in Aflibercept, the application technique is intravitreal injection, when having fewer applications would be related to better adherence to treatment and quality of life, which does not imply that one technology is superior to the other, however the reduction in costs is in favor of Aflibercept, which in units is greater the value but in frequency has an advantage over Ranibizumab.

Anti-VEFG drugs have been shown to be effective treatments against Wet-AMD, the values per billed unit are lower in Ranbizumab, however Aflibercept may have alternative treatment schemes to the monthly sequence with maintenance of clinical results, sequences that may have lower cost are evidenced than Ranibizumab with lower doses applied, improving quality of life and adherence to patients, which infers a better cost-effectiveness ratio. The adjusted values should be monitored to evaluate the relationship in the future as there are other factors that can influence the cost of the compared technologies.

## References bibliographic

1. Hobbs S, Pierce K. Wet age-related macular degeneration (Wet AMD). Florida, EE. UU: Stat Pearls Publishing; 2024 [access 22/02/24]. Available in: https://www.ncbi.nlm.nih.gov/books/NBK572147/

2. Sánchez J. Cost-minimization analysis of ranibizumab versus aflibercept in the treatment of neovascular age-related macular degeneration in Colombia. Ophthalmic Epidemiology. 2020;27(6)482-86. DOI: 10.1080/09286586.2020.1783687.

3. Mitchell P, Annemans L, White R, Gallagher M, Thomas, S. Cost Effectiveness of Treatments for Wet Age-Related Macular Degeneration. Pharmacoeconomics. 2011:29(2):107-3. DOI: 10.2165/11585520-000000000-00000.

4. Deng Y, Qiao L, D, M, Q, C, Wan L, Li J, & Huang L. Age-related macular degeneration: Epidemiology, genetics, pathophysiology, diagnosis, and targeted therapy. Genes & diseases. 2022;9(1):62-79 DOI: 10.1016/j.gendis.2021.02.009.

5. Zhang L, Xie J, Li D, Hu Q, Li X, He R. Conbercept for patients with age-related macular degeneration: a systematic review. BMC Ophthalmolog. 2018;18(1):142 DOI: 10.1186/s12886-018-0807-1

6. Vaidyanathan U, Moshirfar M. NCBI Ranibizumab. Retrieved from Mechanism of Action. 2021 [access 22/02/24];7:25. Available in: https://www.ncbi.nlm.nih.gov/books/NBK544362/

7. Musiał M, Polanowska K, Dobrowolski D, Krysik K, Wylęgała E, Grabarek B, *et al*. A. The effectiveness of brolucizumab and aflibercept in patients with neovascular age-related macular degeneration. International Journal of Environmental Research and Public Health. 2022;19(4):2303. DOI: 10.3390/ijerph19042303

8. Kvannl, L, Krohn J. Switching from pro re nata to treat-and-extend regimen improves visual acuity in patients with neovascular age-related macular degeneration. Acta Ophthalmol. 2027:678-82. DOI: 10.1111/aos.13356

9. Ba J, Peng R, Xu D, Li Y, Shi H, Wang Q, Yu J. Intravitreal anti-VEGF injections for treating wet age-related macular degeneration: a systematic review and meta-analysis. Drug Des Devel Therv. 2015;28:9:5397-405. DOI: 10.2147/DDDT.S86269.

10.Sarwar S, Clearfield E, Soliman M. Afliberce pt for neovascular age-related macular degeneration. The Cochrane database of systematic review. 2016:1-55. DOI: 10.1002/14651858.CD011346.pub2

11. Regnier S, Alsop J, Wrigh, J, Nixon R, Staines H, Fajnkuchen F. Review and comparison of methodologies for indirect comparison of clinical trial results: an illustration with ranibizumab and aflibercept. Expert Rev Pharmacoeconomic Outcomes Res. 2016;16(6):793-801. DOI: 10.1586/14737167.2016.1165609

12. Zhang Y, Chioreso C, Schweizer M, Abràmoff M. Effects of Aflibercept for Neovascular Age-Related Macular Degeneration: A Systematic Review and Meta-Analysis of Observational Comparative Studies. Invest Ophthalmol Vis Sci. 2017:58(13):5616–27 DOI: 10.1167/iovs.17-22471.

13.Empeslidis T, Storey M, Giannopoulos T, Konidaris V, Tranos P, Panagiotou E, *et al.* How Successful is Switching from Bevacizumab or Ranibizumab to Aflibercept in Age-Related Macular Degeneration? A Systematic Overview. Adv Ther. 2019:36(7):1532–48. DOI: 10.1007/s12325-019-00971-0.

14. Plyukhova A, Budzinskaya M, Starostin K, Rejda R, Bucolo C, Reibaldi M, *et al*. Comparative Safety of Bevacizumab, Ranibizumab, and Aflibercept for Treatment of Neovascular Age-Related Macular Degeneration (AMD): A Systematic Review and Network Meta-Analysis of Direct Comparative Studies. J Clin Med. 2020;9(5):1522 DOI: 10.3390/jcm9051522

15. Ohji M, Lanzetta P, Korobelnik JF, Wojciechowski P, Taieb V, Deschaseaux C, *et al*. Efficacy and Treatment Burden of Intravitreal Aflibercept Versus Intravitreal Ranibizumab Treat-and-Extend Regimens at 2 Years: Network Meta-Analysis Incorporating Individual Patient Data Meta-Regression and Matching-Adjusted Indirect Comparison. Adv Ther. 2020;37(5):2184-98. DOI: 10.1007/s12325-020-01298-x.

16. Mejia PA. Estimación de la inflación en el área de la salud que se ajuste a la realidad de consumos de medicamentos, tecnologías y servicios en salud en colombia, 2020. [Tesis de Maestría] [Bogotá, Colombia] Universidad Antonio Nariño, Facultad de Ciencias Económicas y Administrativas; 2022 [access 22/02/24]. Available in: http://repositorio.uan.edu.co/handle/123456789/6558

17. Husereau D, Drummond M, Augustovski F, de Bekker E, Briggs A, Carswel C, *et al.* Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. International journal of technology assessment in health care. Value Health. 2022;25(1):3-9. DOI: 10.1016/j.jval.2021.11.1351.

18. Heie J, Brown D, Chon V, Korobelnik J, Kaiser P, Nguye G. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology. 2012;119(12):2537–48. DOI: 10.1016/j.ophtha.2012.09.006

19. Ohji M, Takahashi K, Okada A, Kobayashi M, Matsuda Y, Terano Y. Efficacy and Safety of Intravitreal Aflibercept Treat-and-Extend Regimens in Exudative Age-Related Macular Degeneration: 52- and 96-Week Findings from ALTAIR. Adv Ther. 2020;37(3):1173–87. DOI: 10.1007/s12325-020-01236-x

20. American Academy of Ophthalmology. Recent Advances in the Management of Age-related Macular Degeneration: What to Expect Over the Next Few Years. Toronto: University of Toronto, 2017. Optom Vis Sci. 2002;79(4):218-24. DOI: 10.1097/00006324-200204000-00008.

## Declaration on interest

The authors declare that they have no conflict of interest.

## Authors' contribution

*Conceptualized:* Ariel Emilio Cortés Martínez, Sahir Camilo Basto Fajardo.

*Designed the methodology:* Carmen Elisa Becerra Huertas, Sahir Camilo Basto Fajardo.

*Software and data curation:* Carmen Elisa Becerra Huertas, Sahir Camilo Basto Fajardo.

*Performed the formal analysis and experiments:* Ariel Emilio Cortés Martínez, Sahir Camilo Basto Fajardo.

*Collected the data.* Sahir Camilo Basto Fajardo.

*Wrote the initial draft and supervised the research*: Ariel Emilio Cortés Martínez, Carmen Elisa Becerra Huertas.

*Prepared the data presentation.* Sahir Camilo Basto Fajardo, Carmen Elisa Becerra Huertas

*Coordinated the project*. Ariel Emilio Cortés Martínez.