Expert consensus

DOI: https://doi.org/10.31288/Ukr.j.ophthalmol.202627176

Sustained disease control with aflibercept 8 mg: A turning point in the management of exudative retinal disease

Working Group:

Andrii R. Korol	Dr Sc (Med), Prof. and Head of Laser Research Department, Filatov Institute of Eye Diseases and Tissue Therapy
Iryna M. Bezkorovaina	Dr Sc (Med), Prof., Department of Otolaryngology and Ophthalmology, Poltava State Medical University
Nataliia M. Veselovska	Dr Sc (Med), Prof., Department of Surgery, Private Higher Educational Establishment Kyiv Medical University
Ganna V. Zaichenko	Dr Sc (Med), Prof. and Head, Pharmacology Department, Bogomolets National Medical University
Nina S. Lutsenko	Dr Sc (Med), Prof. and Head, Surgery Department 1, Educational and Scientific Institute of Postgraduate Education, Zaporizhzhia State Medical and Pharmaceutical University
Oleksii O. Putiienko	Dr Sc (Med), Prof. and Head, Ophthalmology Department, Shupyk National Healthcare University of Ukraine
Andrii M. Sergiienko	Dr Sc (Med) and Prof., Private Institution of Higher Education Dobrobut Academy Medical School, Professor Sergiienko Eye Clinic
Nadiia A. Ulianova	Dr Sc (Med), Prof. and Head, Department of Posttraumatic Eye Pathology, Glaucoma and Lens Pathology, Filatov Institute of Eye Diseases and Tissue Therapy
Valerii D. Beliaiev	Cand Sc (Med) and Ass. Prof., Surgery Department, Faculty of Postgraduate Education and Pre-University Education, Uzhhorod National University
Oleksndra B. Pavliv	Cand Sc (Med) and Head, Ophthalmology Department, Lviv Regional Clinical Hospital
Diana A. Chichur	Cand Sc (Med) and Head, Vitreoretinal Department, Visiobud Eye Clinic
Vasyl I. Shevchyk	Cand Sc (Med), Founder and Surgeon-in-Chief, Vasyl Shevchyk Eye Microsurgery Clinic

Leading Ukrainian retinal disease specialists participated in the Advisory Board meeting held in Kyiv in late September 2025. The meeting aimed to determine the optimal approaches to using aflibercept 8 mg in Ukraine for sustained control of, and best possible treatment outcomes for patients with, exudative retinal disease. This paper contains all the key recommendations for which all the participants achieved consensus after discussion.

Pharmacological properties of aflibercept

Aflibercept is a fully human recombinant fusion protein of domain 2 of vascular endothelial growth factor (VEGF) receptor 1 and domain 3 of VEGF receptor 2 with the Fc fragment of immunoglobulin (IgG)1 [1]. When compared to molecules of other anti-VEGF drugs, the molecule of aflibercept:

- Exhibits higher activity (the half-maximal inhibitory concentration value IC50 = 2.42 nM) [2]
- Exhibits stronger binding to VEGF-A165 (KD = 0.172 pM) [2,3]
- Has an increased number of targets for binding (VEGF-A, VEGF-B, placental growth factor (PlGF), Gal-1) [1,4]
- Exhibits reduced immunogenicity (not more than 3%) [5]

An increase in the molar dose of aflibercept from 2 mg to 8 mg provides for a 34% reduction in the rate of drug clearance from the eye, thus leading to a longer drug affect and allowing for a reduced frequency of intravirtreal drug injections [1].

Aflibercept, a standard of treatment for exudative retinal disease

Aflibercept is considered a standard of care for exudative retinal diseases [6]. Most ophthalmologists in Ukraine prescribe aflibercept as a first-line treatment for such disorders as neovascular age-related macular degeneration (nAMD), diabetic macular edema (DME), and central or branch retinal vein occlusion (CRVO or BRVO).

Aflibercept 8 mg is an innovative high-dose aflibercept medication providing for sustained disease control, with a longer drug affect allowing for a reduced frequency of intravirtreal drug injections, which may potentially contribute to reduced patient costs, extended treatment intervals and improved eye clinic capacity.

The European Medicines Agency (EMA) has approved Eylea 8 mg (aflibercept) for treating nAMD and DME, allowing for extended treatment intervals up to 24 weeks [7]. Given the advantages of aflibercept 8 mg, the drug may become a new standard of treatment for exudative retinal diseases in Ukraine.

Primary patients with nAMD/DME

It is recommended to consider aflibercept 8 mg as a treatment of choice in primary patients with nAMD/DME, and, on indication, patients with CRVO or BRVO, given an opportunity for substantial reduction in the number of required intravitreal injections.

Aflibercept 8 mg should be administered with caution in nAMD patients with:

- High retinal pigment epithelium detachment
- Significant choroidal thinning in the eye with nAMD and retinal atrophy in the fellow eye

These patients should be initially treated with aflibercept 2 mg, while other patients with nAMD/DME patients should be initially treated with aflibercept 2 mg.

Treatment regimen of aflibercept 8 mg in primary patients with nAMD/DME

In order to achieve the best possible treatment outcomes for primary patients with nAMD/DME, the dose of each intravitreal aflibercept injection should be 8 mg (70 µL of 114.3 mg/ml solution).

The optimal treatment regimen of aflibercept 8 mg in primary patients with nAMD/DME is as follows:

- Three loading injections at 4 week (~1 month) intervals
- The fourth loading injection 16 weeks (~4 months) after the third
- A monitoring visit may be scheduled 12 weeks (~3 months) after the third injection to assess disease activity, if required:

In the eyes with signs of active disease, the fourth aflibercept 8 mg injection is given during the monitoring visit, and the next injection is scheduled for 12 weeks later

In the eyes without signs of active disease, the fourth injection is not performed during the monitoring visit but scheduled in 4 weeks (i.e., 16 weeks (~4 months) after the third injection).

- When performing the fourth aflibercept injection, disease activity is assessed and the decision on scheduling the next injection is made:

  In the eyes without signs of active disease, the treatment interval is extended by 4 weeks (e.g., from 16 weeks to 20 weeks)

  In the eyes with signs of active disease, the treatment interval is shortened by 2 weeks (e.g., from 16 weeks to 14 weeks)
- In a similar way, disease activity is assessed and the decision on scheduling the next injection (whether to extend the treatment interval by 4 weeks or to shorten it by 2 weeks) is made when performing each subsequent aflibercept injection
- The maximum treatment interval between aflibercept 8 mg injections is 24 weeks (~6 months), and the minimum treatment interval is 8 weeks (~2 months)
- In order to maintain the achieved visual acuity for long time, regular aflibercept injections should be administered as long as possible (for life, if the physician believes it is reasonable and if the patient can afford it).

Figure 1 shows the treatment regimen of aflibercept 8 mg for nAMD/DME.

Criteria for shortening or extending the interval between aflibercept 8 mg injections

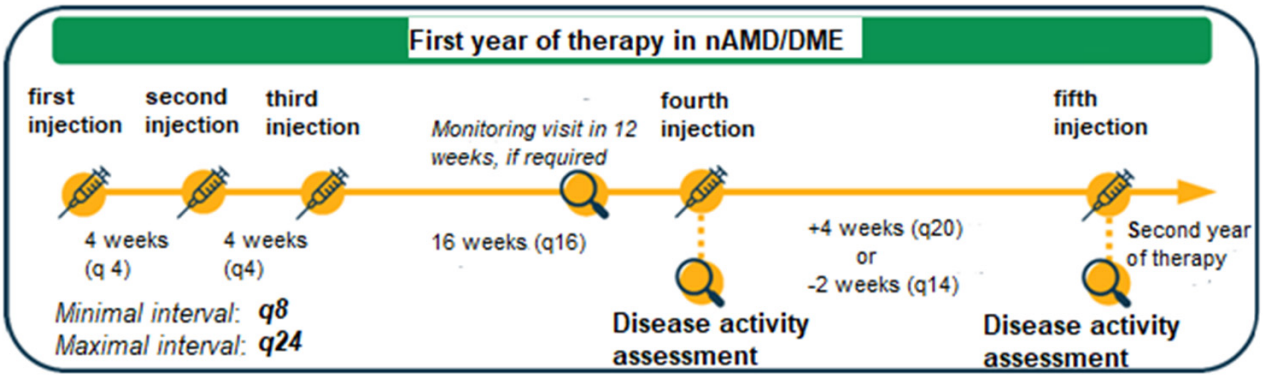

Fig. 1

Disease activity is assessed and the decision on extending or shortening the next injection interval is made according to the criteria established based on the protocols of PULSAR and PHOTON trials. The criteria for extending or shortening the interval have been standardized for nAMD and DME and optimized to simplify their use in routine practice in Ukraine.

Current characteristics are compared with those at the time of making the third injection (i.e., after the initial intensive phase of treatment) while assessing the disease activity.

Criteria for shortening the interval by 2 weeks:

- Visual acuity worsening by more than 1 line

  OR

- An increase in central retinal thickness (CRT) by ≥ 50 μm

Criteria for extending the interval by 4 weeks:

- Stable vision within one acuity line or improvement in vision

  AND

- No change or an increase in CRT by < 50 μm

The criteria are additionally depicted in Fig. 2 for convenience.

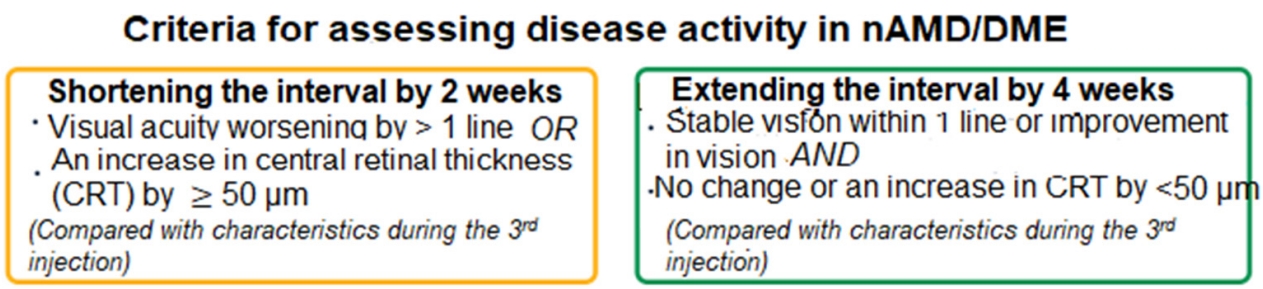

Fig. 2

nAMD/DME patients already receiving anti-VEGF therapy

In nAMD/DME patients already receiving anti-VEGF therapy (aflibercept 2 mg, brolucizumab or faricimab), it is reasonable to consider switching to aflibercept 8 mg, given opportunities for improvement in treatment outcome. To be exact:

- In patients that have achieved an extended interval between anti-VEGF injections (12-16 weeks), given a good response to current treatment, switching to aflibercept 8 mg may allow extending the interval to 24 weeks without efficacy loss
- In patients with insufficient treatment response and/or a short injection interval (< 8 weeks), retinal thickness may be further reduced and residual fluid may be removed by the higher molar dose of aflibercept 8 mg, and the injection interval may be further extended due to a longer treatment effect of aflibercept 8 mg
- In patients with a moderately long interval between anti-VEGF injections (8-10 weeks), switching to aflibercept 8 mg may also allow further extending the interval.

Switching to aflibercept 8 mg from other anti-VEGF therapies

If a decision has been made on switching to aflibercept 8 mg from other anti-VEGF therapies, the optimal switching scheme is as follows:

- If stable vision and CRT and/or an extended interval between anti-VEGF injections (12-16 weeks) were achieved, the first injection of aflibercept 8 mg is performed at the time that has been scheduled for another anti-VEGF injection. The next injection of aflibercept 8 mg is scheduled with the previous interval. When performing the second injection of aflibercept 8 mg, disease activity is assessed and the decision on scheduling the next injection (whether to extend the treatment interval by 4 weeks or to shorten it by 2 weeks) is made
- In patients with lack of response to initial anti-VEGF therapy and/or an interval between initial anti-VEGF injections of <8 weeks, 3 initial injections of aflibercept 8 mg are performed every 4 weeks, with further treatment performed according to the standard aflibercept 8 mg treatment regimen.

The scheme for switching to aflibercept 8 mf from other anti-VEGF therapies is shown in Fig. 3.

Aflibercept 8-mg safety profile

Aflibercept 8 mg demonstrated a favorable safety profile in randomized trials and routine practice which was comparable to that of aflibercept 2 mg [8-11]. Given the above data, the experts believe that (1) wide introduction of aflibercept 8 mg in clinical practice would pose no additional threats, and (2) no measures in addition to standard side effect prevention measures for intravitreal anti-VEGF therapy are required.

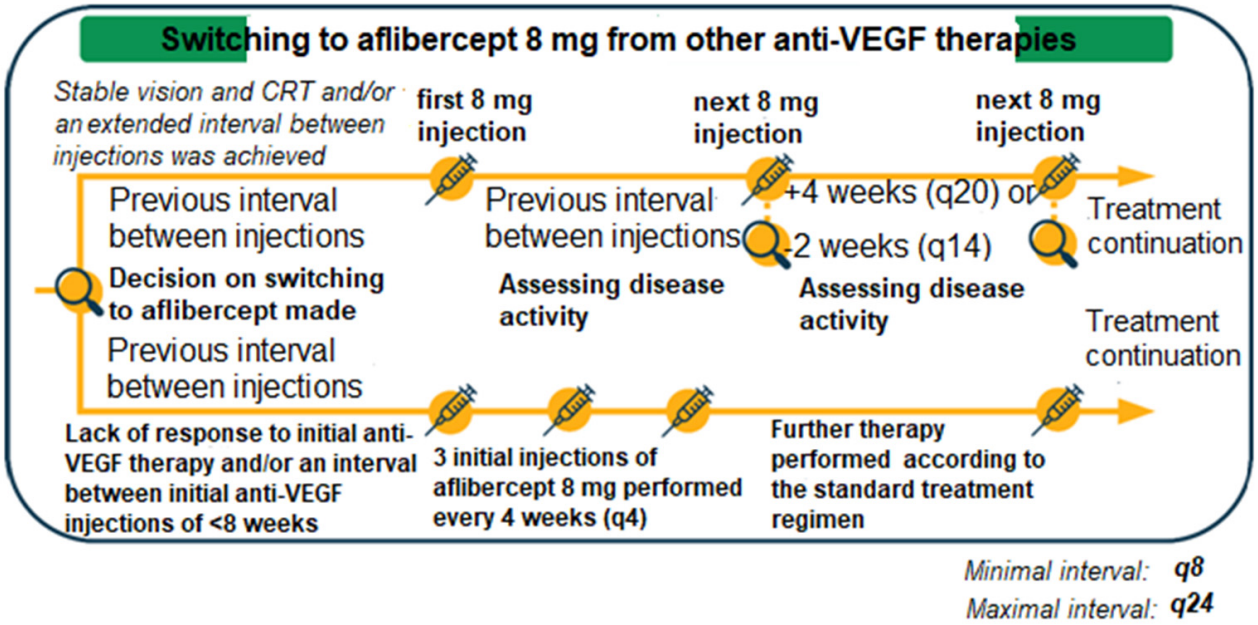

Fig. 3

Conclusion

The appearance of aflibercept 8 mg in Ukraine marked a turning point in the management of exudative retinal disease due to a unique opportunity of extending the interval between injections in nAMD/DME patients to 24 weeks. An increase in the therapeutic drug dose to 8 mg enables extending the effective action to achieve sustained disease control with a favorable safety profile comparable to that of aflibercept 2 mg.

This article was prepared with the support of Bayer

References

1. European Medicines Agency. Assessment report: Eylea. Available at: https://www.ema.europa.eu/en/documents/assessment-report/eylea-epar-public-assessment-report_en.pdf-0. Accessed: October 2025
2. Schubert W, Terjung C, Rafique A, Romano C, Ellinger P, Rittenhouse KD. Evaluation of Molecular Properties versus In Vivo Performance of Aflibercept, Brolucizumab, and Ranibizumab in a Retinal Vascular Hyperpermeability Model. Transl Vis Sci Technol. 2022;11(10):36. doi:10.1167/tvst.11.10.36
3. Regula JT, Lundhvon Leithner P, Foxton R, et al. Targeting key angiogenic pathways with a bispecific CrossMAb optimized for neovascular eye diseases. EMBO Mol Med. 2016;8(11):1265-1288. Published 2016 Nov 2. doi:10.15252/emmm.201505889.
4. Kanda A, Noda K, Saito W, Ishida S. Aflibercept Traps Galectin-1, an Angiogenic Factor Associated with Diabetic Retinopathy. SciRep. 2015;5:17946. Published 2015 Dec 9. doi:10.1038/srep17946.
5. Kim HM, Woo SJ. Immunogenicity and Potential for Intraocular Inflammation of Intravitreal Anti-VEGF Drugs. Curr Ther Res Clin Exp. 2024;100:100742. Published 2024 Mar 14. doi:10.1016/j.curtheres.2024.100742.
6. Sivaprasad S, Ghanchi F, Kelly SP, et al. Evaluation of standard-of-care intravitreal aflibercept treatment practices in patients with diabetic macular oedema in the UK: DRAKO study outcomes. Eye (Lond). 2023;37(12):2527-2534. doi:10.1038/s41433-022-02367-x.

7. Bayer AG. Eylea™ 8 mg with extended 6-month treatment interval approved in the EU. Available at: https://www.bayer.com/media/en-us/eylea-8-mg-with-extended-6-month-treatment-interval-approved-in-the-eu/. Accessed: October 2025.
8. Korobelnik JF, Lanzetta P, Leal S, et al. Intravitreal Aflibercept 8 mg in Neovascular Age-Related Macular Degeneration: Ninety-Six-Week Results from the Randomized Phase 3 PULSAR Trial. Ophthalmology. 2026 Jan;133(1):39-50. doi:10.1016/j.ophtha.2025.08.022
9. Clark WL. Three-year Outcomes of Aflibercept 8mg in Diabetic Macular Edema: Safety and Efficacy Results From the PHOTON Extension Study. Angiogenesis 2025. 8 February 2025. Virtual.
10. Garweg JG, Do DV, Korobelnik JF, et al. A pooled analysis of the CANDELA, PHOTON, and PULSAR trials through 96 weeks: Comparably low intraocular inflammation (IOI)-related events with aflibercept 8 mg and 2 mg. In: Proceedings of the 2025 ARVO Annual Meeting; Salt Lake City, UT, USA. 4–8 May 2025.
11. Konidaris V, Lange C, Munk M, et al. SPECTRUM: early clinical experience from the first global real-world study of aflibercept 8 mg in patients with treatment-naïve neovascular age-related macular degeneration*. In: Proceedings of the 2025 ARVO Annual Meeting; Salt Lake City, UT, USA. 4–8 May 2025.