CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

761355Orig1s000

OTHER REVIEW(S)

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: June 13, 2023

To: Michael Puglisi, Regulatory Health Project Manager
Office of Regulatory Operations
Division of Regulatory Operations for Specialty Medicine (DROSM)

From: Carrie Newcomer, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: James Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for EYLEA HD® (aflibercept) injection, for intravitreal use

BLA: 761355

Background:
In response to DROSM's consult request dated June 1, 2023, OPDP has reviewed the proposed Prescribing Information (PI) and carton and container labeling for the original BLA submission for EYLEA HD® (aflibercept) injection, for intravitreal use.

PI:
OPDP's review of the proposed PI is based on the draft labeling emailed to OPDP on June 1, 2023, and our comments are provided below.

Carton and Container Labeling:
OPDP's review of the proposed carton and container labeling is based on the draft labeling accessed from SharePoint on June 12, 2023, and we do not have any comments at this time.

Thank you for your consult. If you have any questions, please contact Carrie Newcomer at carrie.newcomer@fda.hhs.gov.

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/s/

CARRIE A NEWCOMER
06/13/2023 11:05:54 AM

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	June 12, 2023
Requesting Office or Division:	Division of Ophthalmology (DO)
Application Type and Number:	BLA 761355
Product Name, Dosage Form, and Strength:	Eylea HD[a] (aflibercept)[b] injection, 8 mg/0.07 mL
Applicant/Sponsor Name:	Regeneron Pharmaceuticals, Inc. (Regeneron)
TTT ID #:	2023-3257-1
DMEPA 1 Safety Evaluator:	Damon Birkemeier, PharmD, FISMP, NREMT
DMEPA 1 Team Leader:	Valerie Vaughan, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container labels, carton labeling, and prescribing information (PI) received on June 8, 2023 for Eylea HD. The Division of Ophthalmology (DO) requested that we review the revised container labels, carton labeling, and PI for Eylea HD (Appendix A) to determine if they are acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[c]

2 CONCLUSION

The Applicant implemented all of our recommendations that were shared with them and we have no additional recommendations at this time.

[a] Birkemeier D. Proprietary Name Review for Eylea HD (BLA 761355). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2023 MAR 27. PNR ID No.: 2022-1044724913.
[b] Mena-Grillasca C. Nonproprietary Name Suffix Review for Eylea HD (BLA 761355). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2023 MAY 11. NPNS ID No.: 2022-163.
[c] Birkemeier D. Label and Labeling Review for Eylea HD (BLA 761355). Silver Spring (MD): FDA, CDER, OSE, DMEPA 1 (US); 2023 MAR 29. TTT ID No.: 2023-3257.

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DAMON A BIRKEMEIER
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VALERIE S VAUGHAN
06/12/2023 12:40:45 PM

Clinical Inspection Summary

Date	May 25, 2023
From	Roy Blay, Ph.D. Michele Fedowitz, M.D. Jenn Sellers, M.D., Ph.D. Good Clinical Practice Assessment Branch (GCPAB) Division of Clinical Compliance Evaluation (DCCE) Office of Scientific Investigations (OSI)
To	Wiley Chambers, M.D., Reviewing M.O. Rhea Lloyd, M.D., Clinical Team Leader William Boyd, M.D., Deputy Director Michael Puglisi, P.M. Division of Ophthalmology
BLA	761355
Applicant	Regeneron Pharmaceuticals, Inc.
Drug	Eylea (aflibercept injection) High-Dose 8 mg
NME	No
Therapeutic Classification	VEGF receptor inhibitor
Proposed Indication(s)	Treatment of neovascular (wet) age-related macular degeneration (AMD), diabetic macular edema (DME), and diabetic retinopathy (DR)
Consultation Request Date	15 Feb 2023
Summary Goal Date	9 Jun 2023
Action Goal Date	23 Jun 2023
PDUFA Date	27 Jun 2023

I. OVERALL ASSESSMENT OF FINDINGS AND RECOMMENDATIONS

Clinical data from Protocols 1934 and 20968 were submitted to the Agency in support of BLA 761355 for the use of Eylea (aflibercept) high-dose 8 mg in the treatment of neovascular (wet) age-related macular degeneration (AMD), diabetic macular edema (DME), and diabetic retinopathy (DR). The clinical sites of Drs. Ernest, Win, and Sarrafizadeh were inspected in support of this NDA.

Based on the results of these inspections, Protocols 1934 and 20968 appears to have been conducted adequately and the data generated by these sites appear acceptable in support of the proposed indication.

II. BACKGROUND

The Applicant submitted this BLA to support the use of Eylea high-dose 8 mg for the treatment of neovascular (wet) AMD, DME, and DR. Aflibercept acts as a soluble decoy receptor that binds vascular endothelial growth factor A (VEGF-A) and placental growth factor (PLGF), and thereby can inhibit the binding and activation of these cognate VEGF receptors. Aflibercept by this mechanism inhibits the predominant signaling pathway responsible for angiogenesis and vascular leakage. Eylea (aflibercept) 2 mg was first approved by the FDA on 11 Nov 2011 for treatment of wet AMD, and subsequently approved for treatment of macular edema following retinal vein occlusion, DME, DR, and retinopathy of prematurity.

Inspections of the following protocols were requested in support of this application:

Protocol Number: 1934

Title: A Randomized, Double-Masked, Active-Controlled Phase 2/3 Study of the Efficacy and Safety of High-Dose Aflibercept in Patients with Diabetic Macular Edema

The primary objective of this ongoing Phase 2/3, multi-center, randomized, double-masked study in subjects with DME was to determine if treatment with the Investigational Product (IP), aflibercept high-dose, 8 mg, at intervals of 12 or 16 weeks provided noninferior Best Corrected Visual Acuity (BCVA) compared to 2 mg aflibercept dosed every 8 weeks.

Qualifying subjects were randomized into three treatment groups in a 1:2:1 ratio of those receiving 2 mg aflibercept every eight weeks following five initial monthly doses, aflibercept 8 mg every 12 weeks following three initial monthly doses, or aflibercept 8 mg every 16 weeks following three initial monthly doses. Those subjects receiving 8 mg could undergo drug regimen modification depending upon specific visual and clinical criteria.

The primary efficacy endpoint was the change from baseline in BCVA at Week 48 as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) letter score.

This study was conducted in 138 domestic and foreign centers with 660 randomized subjects. The study began on 29 Jun 2020 (first participant first visit) and the primary completion date was 30 May 2022 (last participant last visit for primary endpoint).

Protocol Number: 20968

Title: Randomized, Double-Masked, Active-Controlled, Phase 3 Study of the Efficacy and Safety of High Dose Aflibercept in Patients with Neovascular Age-Related Macular Degeneration

The primary objective of this Phase 3, multicenter, randomized, double-masked, active-controlled study was to determine whether treatment with aflibercept high-dose at intervals of 12 or 16 weeks provided non-inferior Best Corrected Visual Acuity (BCVA) change compared to aflibercept 2 mg every 8 weeks in participants with wet AMD.

Qualifying subjects with wet AMD were randomized into three treatment groups in a 1:1:1 ratio of those receiving 2 mg aflibercept every eight weeks, 8 mg aflibercept every 12 weeks, or 8 mg aflibercept every 16 weeks. Those subjects receiving 8 mg dosing could undergo drug regimen modification depending upon specific visual and clinical criteria. The primary efficacy endpoint was the change from baseline in BCVA at Week 48 as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) letter score. This study was conducted at 251 domestic and foreign sites with approximately 960 subjects randomized across the three treatment groups. The study began on 24 Apr 2020 (first participant first visit) and the last participant last visit was on 27 Jul 2022 (for the study up to Week 48.

III. RESULTS

Protocol 1934

1. **Jan Ernest, MD**
   Ostrovskeho 3
   Praha 5 150 00
   Czech Republic

   Site: 203504
   Inspection Dates: 19-28 Apr 2023

   Dr. Ernest was inspected for the conduct of Protocol 1934. At this site, 29 subjects were screened, 25 were randomized, 18 subjects completed the study, and seven subjects were terminated early (six deaths and one lost to follow up). The six deaths (Subjects (b) (6) (b) (6)) were reported and appear unrelated to the conduct of the study.

   The primary efficacy endpoint data were verified against the data listings for all 25 randomized subjects except for a discrepancy in BCVA measurement. For Subject (b) (6), the source data recorded a BCVA of 76, while there was no measurement in the data line listings.

   Reviewer Comment: As this was an early time point and not a high-dose treatment, it would seem unlikely to influence efficacy results.

   Adverse events and concomitant medications in the source data for seven subjects were compared with the data listings. Discrepancies were observed that included the following:

Subject	Category	Source Document	Data Line Listings
(b) (6)	Concomitant Medication	Flarex	Not listed
	Adverse Event	Worsening DME (OL)	Not listed

Other discrepancies included instances where pharmacokinetic (PK) sampling was not done and incorrect start/stop dates for some concomitant medications and adverse events.

Reviewer Comment: Subject (b) (6) was treated with an unreported ophthalmic medication and also experienced worsening DME that was not reported. The review division may wish to consider the effect, if any, of this unreported treatment and condition on study outcome. Otherwise, the observed discrepancies appear isolated and would appear not to affect subject safety or study outcome.

Other subject records reviewed included consent forms, demographics, concomitant medications, medical histories, vital signs, physical examinations, BCVA, intraocular pressures (IOPs), slit lamp examinations, National Eye Institute Visual Function Questionnaire-25 (NEI VFQ-25), Drug Regimen Modification (DRM) assessments, Investigational Product (IP) administration, laboratory reports, and progress notes. Study related documents reviewed included Institutional Review Board (IRB) submissions and approvals, site correspondence, monitoring reports, investigational product accountability logs, training records, delegation logs, and financial disclosure forms.

The inspection compared the paper source records with the data listings with some discrepancies observed as described above. Otherwise, adherence to the regulations and the investigational plan appeared adequate.

2. Win, Peter, M.D.
Win Retina
234 S. First Avenue, Suite 101
Arcadia, California, 91006

Site: 840615
Inspection Dates: 17-21 Apr 2023

Dr. Win was inspected for the conduct of Protocol 1934. At this site, 36 subjects were screened, six subjects failed screening, 30 subjects were enrolled, and 27 subjects completed the study with one death (Subject (b) (6) cardio-pulmonary arrest, reported) and two subjects were lost to follow up.

The source records of 21 subjects were reviewed for primary efficacy endpoint and adverse event reporting and verified against the data listings; however, adverse events experienced by Subject (b) (6) (admittance to the ER on (b) (6) for cardiac arrest) and Subject (b) (6) (hospitalization on (b) (6) for COVID/pneumonia) were not reflected in the line listings. Other subject related records reviewed included eligibility criteria, informed consent,

electronic case report forms (eCRFs), and protocol deviations. Study related documents reviewed included IRB submissions and approvals, sponsor and monitor correspondence, investigational product (IP) accountability, training documentation, Form 1572s, delegation logs, and financial disclosure documents.

The inspection compared the source records with the data listings and there were no significant discrepancies other than the adverse events noted above. Otherwise, adherence to the regulations and the investigational plan appeared adequate.

Protocol 20968

1. **Jan Ernest, MD**
   Ostrovskeho 3
   Praha 5 150 00
   Czech Republic

   Site: 38001
   Inspection Dates: 19-28 Apr 2023

   Dr. Ernest was inspected for the conduct of Protocol 20968. At this site 38 subjects were screened, 32 were randomized, six subjects were screen failures, and 27 subjects completed the main study.

   The primary efficacy endpoint data were verified against the data listings for all 32 randomized subjects except for one discrepancy as shown in the table below.

Subject	Arm	BCVA	Source Document	Data Line Listings
(b) (6)	High-Dose 8 mg	Total at Week 48	62 OD	36 OD

Reviewer Comment: The actual visual acuity for Subject (b) (6) *in the source was substantially better than the acuity submitted to the application in the data line listings, making this discrepancy biased against the study drug.*

Adverse events and concomitant medications in the source data for seven subjects were reviewed and compared with the data listings. The following concomitant medications were not reported:

Subject	Concomitant Medications listed in the Source Documents	Data Line Listings
(b) (6)	Xados, Atarax	Not listed
	Trombex	Not listed
	Glucophage XR, Bonviva	Not listed

There was also at least one example of inaccurate end dates for the administration of a concomitant medication.

Reviewer Comment: These discrepancies would appear isolated and not to have a significant effect upon subject safety or study outcome; however, we recommend the review division consider these unreported concomitant medications in the review.

Other subject records reviewed included consent forms, demographics, concomitant medications, medical histories, vital signs, physical examinations, BCVA, IOP, slit lamp examination, NEI VFQ-25, adverse events, DRM assessments, IP administration, and laboratory reports. Study related documents reviewed included Institutional Review Board (IRB) submissions and approvals, site correspondence, monitoring reports, investigational product accountability logs, training records, delegation logs, and financial disclosure forms.

The inspection compared the paper source records with the data listings, with some discrepancies observed as described above. Otherwise, adherence to the regulations and the investigational plan appeared adequate.

2. Ramin Sarrafizadeh, MD
Retina Consultants of Southern CO
2770 North Union Blvd, Suite 140
Colorado Springs, CO

Site: 14062
Inspection Dates: 18-21 Apr 2023

Dr. Sarrafizadeh was inspected for the conduct of Protocol 20968. At this site, 27 subjects were screened, six failed screening, 21 subjects were randomized to the study, four subjects were discontinued from the study, and 17 subjects completed the study.

The primary efficacy endpoint data and adverse events were verified against the source data for all randomized subjects. There were three reports of adverse events captured in the electronic data capture system that were not reflected in the data listings: Subject (b) (6) who experienced nausea and Subject (b) (6) who had COVID-19 and allergies.

Other subject related study records that were reviewed included eligibility, informed consent, concomitant medications, and IP dispensation. Study related documents reviewed included monitor and IRB correspondence, training records, delegation logs, masking status, consent forms, financial disclosure, electronic records, and IP shipment, receipt, and storage records.

The inspection compared the paper source records with the data listings, with minor discrepancies regarding adverse event reporting as described above. Otherwise, adherence to the regulations and the investigational plan appeared adequate.

{See appended electronic signature page}

Roy Blay, Ph.D.
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE: {See appended electronic signature page}

Michele Fedowitz, M.D.
Team Leader,
Good Clinical Practice Assessment Branch
Division of Clinical Compliance Evaluation
Office of Scientific Investigations

CONCURRENCE: {See appended electronic signature page}

Jenn Sellers, M.D., Ph.D., Branch Chief
Good Clinical Practice Assessment Branch
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CC:
Central Doc. Rm.
DO/Division Director/Medical Officer/Wiley Chambers
DO/Deputy Director/William Boyd
DO/Medical Team Leader/Rhea Lloyd
DO/Project Manager/Michael Puglisi
OSI/Office Director/David Burrow
OSI/Deputy Director/Laurie_Muldowney
OSI/DCCE/Division Director/Kassa Ayalew
OSI/DCCE/GCPAB/Branch Chief/Jenn Sellers
OSI/DCCE/GCPAB/Team Leader/Michele Fedowitz
OSI/DCCE/GCPAB Reviewer/Roy Blay
OSI/DCCE/GCPAB/Program Analyst/Yolanda Patague

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ROY A BLAY
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MICHELE B FEDOWITZ
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JENN W SELLERS
05/30/2023 06:44:23 AM

LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis 1 (DMEPA 1)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	March 29, 2023
Requesting Office or Division:	Division of Ophthalmology (DO)
Application Type and Number:	BLA 761355
Product Name and Strength:	aflibercept-xxxx[a] injection, 8 mg/0.07 mL
Product Type:	Single Ingredient Product – Vial Combination Product (Drug-Device) – Vial Kit
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Regeneron Pharmaceuticals, Inc. (Regeneron)
FDA Received Date:	December 27, 2022
TTT ID #:	2023-3257
DMEPA 1 Safety Evaluator:	Damon Birkemeier, PharmD, FISMP, NREMT
DMEPA 1 Team Leader:	Valerie Vaughan, PharmD

[a] The nonproprietary name for this BLA has not yet been determined; therefore, the placeholder "aflibercept-xxxx" is used throughout this review to refer to the non-proprietary name for this product and not intended to be included in the final labels and labeling.

1 REASON FOR REVIEW

As part of the approval process for aflibercept-xxxx injection, the Division of Ophthalmology (DO) requested that we review the proposed container labels, carton labeling, and prescribing information (PI) for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

Table 1. Materials Considered for this Label and Labeling Review	
Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B – N/A
ISMP Newsletters*	C – N/A
FDA Adverse Event Reporting System (FAERS)*	D – N/A
Other	E – N/A
Labels and Labeling	F
N/A=not applicable for this review *We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance	

3 CONCLUSION AND RECOMMENDATIONS

The proposed container label, carton labeling and prescribing information (PI) may be improved to promote the safe use of this product from a medication error perspective. We provide the identified medication error issues, our rationale for concern, and our proposed recommendations to minimize the risk for medication error in Section 4 for the Division and in Section 5 for Regeneron Pharmaceuticals, Inc.

4 RECOMMEDATIONS FOR DIVISION OF OPHTHALMOLOGY (DO)

Table 2. Identified Issues and Recommendations for the Division of Ophthalmology (DO)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Prescribing Information – General Issues			
1.	We note that the indication “neovascular (wet) age-related	It is unclear if the appropriate abbreviation	We defer to the Division to determine the appropriate abbreviation for the indication

Table 2. Identified Issues and Recommendations for the Division of Ophthalmology (DO)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
	macular degeneration" is abbreviated as "nAMD". However, in other Prescribing Information for products used to treat neovascular (wet) age-related macular degeneration, it is abbreviated as "AMD".	for this indication is nAMD *versus* AMD.	"neovascular (wet) age-related macular degeneration".
Full Prescribing Information – Section 2 Dosage and Administration			
1.	We note dosages are described using multiple units of measurement.	Concurrent use of multiple units of measurement (i.e., mg, mL, and microliters) increases the risk of confusion and could lead to medication dosing errors.[b]	We recommend revising the dosing recommendations to remove dosage described in terms of mL and microliters. For example, revise to: "The recommended dose for Eylea HD is 8 mg administered via intravitreal injection every 4 weeks (monthly, approximately every 28 days ± 7 days,) for the first three doses, followed by 8 mg via intravitreal injection once every 8 to 16 weeks (2 to 4 months ± 7 days)".
Full Prescribing Information – Section 16 How Supplied/Storage and Handling			
1.	As currently presented, the appropriate information to facilitate identification of the dosage form is not included.	Section 16 *How Supplied/Storage and Handling* should contain information suitable for product identification in accordance with 21 CFR 201.57(c)(17)(iii).	We recommend including identifying information in Section 16 *How Supplied/Storage and Handling* (e.g., Eylea HD is a clear, colorless to pale yellow solution).

[b] Guidance for Industry: *Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors.* 2022. Available from https://www.fda.gov/media/158522/download.

5 RECOMMENDATIONS FOR REGENERON PHARMACEUTICALS, INC.

Table 3. Identified Issues and Recommendations for Regeneron Pharmaceuticals, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label			
1.	The discard statement "Discard unused portion" is not present next to the package type term "single-dose vial".	Inclusion of this discard statement helps minimize the risk of the entire contents of the vial being given as a single dose when a dose volume less than the entire contents is intended.	We recommend revising the statement "Single-Dose Vial" to read as "Single-Dose Vial. Discard Unused Portion". See *Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018)*.
Carton Labeling			
1.	The terminology "(b) (4)" within the recommended dosage statement is inconsistent with the Prescribing Information.	To ensure consistency with the prescribing information.	Revise "Dosage and Administration: (b) (4) to read "Dosage and Administration: See prescribing information." Additionally, revise "(b) (4) " in the "carton contents" statement to "Prescribing Information."
2.	The discard statement "Discard unused portion" is not present next to the package type term "single-dose vial".	Inclusion of this discard statement helps minimize the risk of the entire contents of the vial being given as a single dose when a dose volume less than the entire contents is intended.	We recommend revising the statement "Single-Dose Vial" to read as "Single-Dose Vial. Discard Unused Portion". See *Guidance for Industry: Selection of the Appropriate Package Type Terms and Recommendations for Labeling*

Table 3. Identified Issues and Recommendations for Regeneron Pharmaceuticals, Inc. (entire table to be conveyed to Applicant)			
	IDENTIFIED ISSUE	RATIONALE FOR CONCERN	RECOMMENDATION
Container Label			
			Injectable Medical Products Packaged in Multiple-Dose, Single-Dose, and Single-Patient-Use Containers for Human Use (October 2018).
3.	The phrase "(b) (4) [redacted]" statement includes two units of measurement	We note "(b) (4)" is not a common terminology of measurement on syringes, and the syringe provided in the kit measures in "mL".	We recommend removing the reference to "(b) (4)" from this statement.

APPENDICIES: METHODS & RESULTS FOR EACH MATERIAL REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table presents relevant product information for aflibercept-xxxx that Regeneron Pharmaceuticals, Inc. submitted on December 27, 2022.

Table 4. Relevant Product Information for aflibercept-xxxx	
Initial Approval Date	N/A
Active Ingredient	Aflibercept-xxxx
Indication	• Neovascular (Wet) Age-Related Macular Degeneration (nAMD) • Diabetic Macular Edema (DME) • Diabetic Retinopathy (DR)
Route of Administration	Intravitreal
Dosage Form	Injection
Strength	8 mg/0.07 mL
Dose and Frequency	(b) (4)
How Supplied	Single-use vials supplied in the following presentations: • Vial kit with injection components o One single-dose glass vial o One 18-gauge x 1½-inch, 5-micron, filter needle for withdrawal of the vial contents o One 30-gauge x ½-inch injection needle for intravitreal injection o One 1 mL syringe for administration o One package insert • Vial only o One single-dose glass vial o One Prescribing Information
Storage	Refrigerate at 2°C to 8°C (36°F to 46°F). Do not freeze. Store in the original carton until time of use to protect from light

APPENDIX F. LABELS AND LABELING

F.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[c] along with postmarket medication error data, we reviewed the following Eylea HD labels and labeling submitted by Regeneron Pharmaceuticals, Inc. submitted on December 27, 2022.

- Container labels
- Carton labeling
- Professional Sample Container Label
- Professional Sample Carton Labeling
- Instructions for Use (IFU) (Image not shown) available in the PI
- Prescribing Information (PI) (Image not shown) available from \\CDSESUB1\EVSPROD\bla761355\0001\m1\us\114-labeling\draft\annotated\annotated.pdf

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[c] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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DAMON A BIRKEMEIER
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VALERIE S VAUGHAN
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