OPHTHALMOLOGIC POLICY: VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) INHIBITORS

Policy Number: 2019D0042L **Effective Date**: March 1, 2019

Instructions for Use

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COVERAGE RATIONALE

See Benefit Considerations

This policy provides information about the use of certain specialty pharmacy medications administered by the intravitreal route for ophthalmologic conditions.

This policy refers to the following drug products, all of which are vascular endothelial growth factor (VEGF) inhibitors:

- Eylea™ (aflibercept)
- Avastin® (bevacizumab)
- Macugen® (pegaptanib)
- Lucentis® (ranibizumab)

Proven

I. **Eylea (aflibercept) is proven and medically necessary for the treatment of**:
   A. Neovascular age-related macular degeneration (AMD)
   B. Diabetic macular edema (DME)
   C. Macular edema secondary to branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO)
   D. Diabetic retinopathy in patients with diabetic macular edema (DME)

II. **Avastin (bevacizumab) is proven and medically necessary for the treatment of**:
   A. Neovascular age-related macular degeneration (AMD)
   B. Diabetic macular edema
   C. Macular edema secondary to branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO)
   D. Proliferative diabetic retinopathy
   E. Neovascular glaucoma
   F. Choroidal neovascularization secondary to pathologic myopia, angioid streaks/pseudoxanthoma elasticum, or ocular histoplasmosis syndrome (OHS)

III. **Macugen (pegaptanib) is proven and medically necessary for the treatment of**:
   A. Neovascular age-related macular degeneration (AMD)
   B. Diabetic macular edema

IV. **Lucentis (ranibizumab) is proven and medically necessary for the treatment of**:
   A. Neovascular age-related macular degeneration (AMD)
   B. Diabetic macular edema (DME)
   C. Macular edema secondary to branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO)

D. Choroidal neovascularization secondary to pathologic myopia, angioid streaks/pseudoxanthoma elasticum, or ocular histoplasmosis syndrome (OHS)
E. Diabetic retinopathy

Additional Information

Avastin (bevacizumab) is supplied in sterile vials containing a solution of 25 mg/mL. Doses utilized in ophthalmic conditions generally range from 6.2 mcg to 2.5 mg. Therefore, bevacizumab in vials is often divided into single-dose, prefilled syringes for intravitreal use by compounding pharmacies. Compounding pharmacies must comply with United States Pharmacopeia (USP) Chapter 797, which sets standards for the compounding, transportation, and storage of compounded sterile products (CSP).[1] The Pharmacy Compounding Accreditation Board can verify that the pharmacy is adhering to these standards.[2]

The American Society of Retinal Specialists (ASRS) is committed to ensuring that retina specialists have access to compounded drugs (such as Avastin) that are prepared with high-quality material following good quality controls and sound engineering design by appropriately trained personnel. Please refer to their information page at https://www.asrs.org/advocacy-practice/access-to-safe-compounded-agents for resources pertaining to access of safe compounded agents.[14]

Please refer to the US Food and Drug Administration (FDA) Section of this policy for information related to contamination of compounded bevacizumab. In an effort to guard against contamination during the compounding process, the United States Veterans Health Administration (USVHA) requires that only USVHA pharmacies may dispense bevacizumab for intravitreal administration to Veterans Administration beneficiaries. The medication must be dispensed directly to the VA ophthalmologist, who will then be responsible for preparing and administering the bevacizumab dose for each patient. In addition to strict labeling and storage requirements, the ophthalmologist is required to prepare only one dose of medication from each vial; if both eyes are to be treated, a separate vial and syringe must be utilized.[3]

U.S. FOOD AND DRUG ADMINISTRATION (FDA)

Avastin (bevacizumab)

The statements below are for information only. Oncology indications for bevacizumab are listed in the NCCN Drugs & Biologics Compendium.

- Bevacizumab, in combination with intravenous 5-fluorouracil–based chemotherapy, is indicated for first- or second-line treatment of patients with metastatic carcinoma of the colon or rectum.[57]
- Bevacizumab, in combination with fluoropyrimidine- irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients with metastatic colorectal cancer who have progressed on a first-line bevacizumab-containing regimen.[57]
- Bevacizumab, in combination with carboplatin and paclitaxel, is indicated for first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous, non-small cell lung cancer.[57]
- Bevacizumab for treatment of glioblastoma, is indicated as a single agent for patients with progressive disease following prior therapy.[57]
- Bevacizumab, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic cervical cancer.[57]
- Bevacizumab, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma.[57]
- Bevacizumab, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.[57]
- Bevacizumab, in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine, followed by bevacizumab as a single agent, is indicated for the treatment of platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.[57]
- Bevacizumab, in combination with carboplatin and paclitaxel, followed by bevacizumab as a single agent, for stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection.[57]
- Bevacizumab, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received no more than 2 prior chemotherapy regimens.[57]

Administration of bevacizumab infusions or intravitreal injections for the treatment of ophthalmologic conditions is considered off-label.

The FDA issued an alert dated August 30, 2011 that notification had been received from the Florida Department of Health (DOH) regarding a cluster of *Streptococcus endophthalmitis* infections in three clinics following intravitreal injection of repackaged Avastin.[58] Investigators traced the tainted injections to a single pharmacy that had repackaged the Avastin from sterile injectable 100 mg/4 mL, single-use, preservative-free vials into individual 1 mL

single-use syringes. The alert reminded health care professionals that repackaging sterile drugs without proper aseptic technique can compromise product sterility, potentially putting the patient at risk for microbial infections. Health care professionals should ensure that drug products are obtained from appropriate, reliable sources and properly administered.

Eylea (aflibercept)

Aflibercept is indicated for the treatment of patients with neovascular (wet) age-related macular degeneration (AMD), macular edema following retinal vein occlusion (RVO), diabetic macular edema (DME), and diabetic retinopathy in patients with DME.[5]

Lucentis (ranibizumab)

Ranibizumab is indicated for the treatment of patients with neovascular (wet) age-related macular degeneration (AMD), macular edema following retinal vein occlusion (RVO), diabetic macular edema (DME), and diabetic retinopathy.[7]

Macugen (pegaptanib)

Pegaptanib is indicated for the treatment of patients with neovascular (wet) age-related macular degeneration (AMD).[6]

BACKGROUND

Vascular endothelial growth factor (VEGF) is a protein that stimulates the growth, proliferation and survival of vascular endothelial cells. VEGF plays a critical role in the development of new blood vessels (angiogenesis), increases vascular permeability in small blood vessels and prevents apoptosis of vascular endothelial cells in immature blood vessels. VEGF has been implicated in blood retinal barrier breakdown and pathological ocular neovascularization.[4]

APPLICABLE CODES

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Coverage Determination Guidelines may apply.

HCPCS Code	Description	Brand Name
J0178	Injection, aflibercept, 1 mg	Eylea
J2503	Injection, pegaptanib sodium, 0.3 mg	Macugen
J2778	Injection, ranibizumab, 0.1 mg	Lucentis
J9035	Injection, bevacizumab, 10 mg	Avastin

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
B39.4	Histoplasmosis capsulati, unspecified			x	x
B39.5	Histoplasmosis duboisii			x	x
B39.9	Histoplasmosis, unspecified			x	x
E08.311	Diabetes mellitus due to underlying condition with unspecified diabetic retinopathy with macular edema		x	x	x
E08.319	Diabetes mellitus due to underlying condition with unspecified diabetic retinopathy without macular edema			x	
E08.3211	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, right eye		x	x	x
E08.3212	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, left eye		x	x	x
E08.3213	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, bilateral		x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E08.3219	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E08.3291	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy without macular edema, right eye		x	x	x
E08.3292	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy without macular edema, left eye		x	x	x
E08.3293	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy without macular edema, bilateral		x	x	x
E08.3299	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye		x	x	x
E08.3311	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, right eye		x	x	x
E08.3312	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, left eye		x	x	x
E08.3313	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, bilateral		x	x	x
E08.3319	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E08.3391	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy without macular edema, right eye		x	x	x
E08.3392	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy without macular edema, left eye		x	x	x
E08.3393	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy without macular edema, bilateral		x	x	x
E08.3399	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye		x	x	x
E08.3411	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, right eye		x	x	x
E08.3412	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, left eye		x	x	x
E08.3413	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, bilateral		x	x	x
E08.3419	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E08.3491	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy without macular edema, right eye		x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E08.3492	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy without macular edema, left eye		x	x	x
E08.3493	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy without macular edema, bilateral		x	x	x
E08.3499	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye		x	x	x
E08.3511	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, right eye		x	x	x
E08.3512	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, left eye		x	x	x
E08.3513	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, bilateral		x	x	x
E08.3519	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E08.3521	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye		x	x	x
E08.3522	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye		x	x	x
E08.3523	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral		x	x	x
E08.3529	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment involving the macula, unspecified eye		x	x	x
E08.3531	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye		x	x	x
E08.3532	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye		x	x	x
E08.3533	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral		x	x	x
E08.3539	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye		x	x	x
E08.3541	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye		x	x	x
E08.3542	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye		x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E08.3543	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral		x	x	x
E08.3549	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye		x	x	x
E08.3551	Diabetes mellitus due to underlying condition with stable proliferative diabetic retinopathy, right eye		x	x	x
E08.3552	Diabetes mellitus due to underlying condition with stable proliferative diabetic retinopathy, left eye		x	x	x
E08.3553	Diabetes mellitus due to underlying condition with stable proliferative diabetic retinopathy, bilateral		x	x	x
E08.3559	Diabetes mellitus due to underlying condition with stable proliferative diabetic retinopathy, unspecified eye		x	x	x
E08.3591	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema, right eye			x	x
E08.3592	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema, left eye			x	x
E08.3593	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema, bilateral			x	x
E08.3599	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema, unspecified eye			x	x
E08.37X1	Diabetes mellitus due to underlying condition with diabetic macular edema, resolved following treatment, right eye			x	x
E08.37X2	Diabetes mellitus due to underlying condition with diabetic macular edema, resolved following treatment, left eye			x	x
E08.37X3	Diabetes mellitus due to underlying condition with diabetic macular edema, resolved following treatment, bilateral			x	x
E08.37X9	Diabetes mellitus due to underlying condition with diabetic macular edema, resolved following treatment, unspecified eye			x	x
E09.311	Drug or chemical induced diabetes mellitus with unspecified diabetic retinopathy with macular edema		x	x	x
E09.3211	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye		x	x	x
E09.3212	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye		x	x	x
E09.3213	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral		x	x	x
E09.3219	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E09.3291	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye		x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E09.3292	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye		x	x	x
E09.3293	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral		x	x	x
E09.3299	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye		x	x	x
E09.3311	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye		x	x	x
E09.3312	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye		x	x	x
E09.3313	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral		x	x	x
E09.3319	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E09.3391	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye		x	x	x
E09.3392	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye		x	x	x
E09.3393	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral		x	x	x
E09.3399	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye		x	x	x
E09.3411	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye		x	x	x
E09.3412	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye		x	x	x
E09.3413	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral		x	x	x
E09.3419	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E09.3491	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye		x	x	x
E09.3492	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye		x	x	x
E09.3493	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral		x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E09.3499	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye		x	x	x
E09.3511	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye		x	x	x
E09.3512	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye		x	x	x
E09.3513	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral		x	x	x
E09.3519	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E09.3521	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye		x	x	x
E09.3522	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye		x	x	x
E09.3523	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral		x	x	x
E09.3529	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, unspecified eye		x	x	x
E09.3531	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye		x	x	x
E09.3532	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye		x	x	x
E09.3533	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral		x	x	x
E09.3539	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye		x	x	x
E09.3541	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye		x	x	x
E09.3542	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye		x	x	x
E09.3543	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral		x	x	x
E09.3549	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye		x	x	x
E09.3551	Drug or chemical induced diabetes mellitus with stable proliferative diabetic retinopathy, right eye		x	x	x
E09.3552	Drug or chemical induced diabetes mellitus with stable proliferative diabetic retinopathy, left eye		x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E09.3553	Drug or chemical induced diabetes mellitus with stable proliferative diabetic retinopathy, bilateral		x	x	x
E09.3559	Drug or chemical induced diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye		x	x	x
E09.3591	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye			x	x
E09.3592	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye			x	x
E09.3593	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral			x	x
E09.3599	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye			x	x
E09.37X1	Drug or chemical induced diabetes mellitus with diabetic macular edema, resolved following treatment, right eye			x	x
E09.37X2	Drug or chemical induced diabetes mellitus with diabetic macular edema, resolved following treatment, left eye			x	x
E09.37X3	Drug or chemical induced diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral			x	x
E09.37X9	Drug or chemical induced diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye			x	x
E10.311	Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema	x	x	x	x
E10.3211	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye	x	x	x	x
E10.3212	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye	x	x	x	x
E10.3213	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral	x	x	x	x
E10.3219	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye	x	x	x	x
E10.3291	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye	x	x	x	x
E10.3292	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye	x	x	x	x
E10.3293	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral	x	x	x	x
E10.3299	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye	x	x	x	x
E10.3311	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye	x	x	x	x
E10.3312	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye	x	x	x	x
E10.3313	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral	x	x	x	x
E10.3319	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye	x	x	x	x
E10.3391	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye	x	x	x	x
E10.3392	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye	x	x	x	x
E10.3393	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral	x	x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E10.3399	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye	x	x	x	x
E10.3411	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye	x	x	x	x
E10.3412	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye	x	x	x	x
E10.3413	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral	x	x	x	x
E10.3419	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye	x	x	x	x
E10.3491	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye	x	x	x	x
E10.3492	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye	x	x	x	x
E10.3493	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral	x	x	x	x
E10.3499	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye	x	x	x	x
E10.3511	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye	x	x	x	x
E10.3512	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye	x	x	x	x
E10.3513	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral	x	x	x	x
E10.3519	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye	x	x	x	x
E10.3521	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye	x	x	x	x
E10.3522	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye	x	x	x	x
E10.3523	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral	x	x	x	x
E10.3529	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, unspecified eye	x	x	x	x
E10.3531	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye	x	x	x	x
E10.3532	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye	x	x	x	x
E10.3533	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral	x	x	x	x
E10.3539	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye	x	x	x	x
E10.3541	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye	x	x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E10.3542	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye	x	x	x	x
E10.3543	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral	x	x	x	x
E10.3549	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye	x	x	x	x
E10.3551	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, right eye	x	x	x	x
E10.3552	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, left eye	x	x	x	x
E10.3553	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral	x	x	x	x
E10.3559	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye	x	x	x	x
E10.3591	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye			x	x
E10.3592	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye			x	x
E10.3593	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral			x	x
E10.3599	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye			x	x
E10.37X1	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye			x	x
E10.37X2	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye			x	x
E10.37X3	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral			x	x
E10.37X9	Type 1 diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye			x	x
E11.311	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema	x	x	x	x
E11.3211	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye	x	x	x	x
E11.3212	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye	x	x	x	x
E11.3213	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral	x	x	x	x
E11.3219	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye	x	x	x	x
E11.3291	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye	x	x	x	x
E11.3292	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye	x	x	x	x
E11.3293	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral	x	x	x	x
E11.3299	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye	x	x	x	x
E11.3311	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye	x	x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E11.3312	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye	x	x	x	x
E11.3313	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral	x	x	x	x
E11.3319	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye	x	x	x	x
E11.3391	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye	x	x	x	x
E11.3392	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye	x	x	x	x
E11.3393	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral	x	x	x	x
E11.3399	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye	x	x	x	x
E11.3411	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye	x	x	x	x
E11.3412	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye	x	x	x	x
E11.3413	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral	x	x	x	x
E11.3419	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye	x	x	x	x
E11.3491	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye	x	x	x	x
E11.3492	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye	x	x	x	x
E11.3493	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral	x	x	x	x
E11.3499	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye	x	x	x	x
E11.3511	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye	x	x	x	x
E11.3512	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye	x	x	x	x
E11.3513	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral	x	x	x	x
E11.3519	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye	x	x	x	x
E11.3521	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye	x	x	x	x
E11.3522	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye	x	x	x	x
E11.3523	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral	x	x	x	x
E11.3529	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, unspecified eye	x	x	x	x
E11.3531	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye	x	x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E11.3532	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye	x	x	x	x
E11.3533	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral	x	x	x	x
E11.3539	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye	x	x	x	x
E11.3541	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye	x	x	x	x
E11.3542	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye	x	x	x	x
E11.3543	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral	x	x	x	x
E11.3549	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye	x	x	x	x
E11.3551	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, right eye	x	x	x	x
E11.3552	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, left eye	x	x	x	x
E11.3553	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral	x	x	x	x
E11.3559	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye	x	x	x	x
E11.3591	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye			x	x
E11.3592	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye			x	x
E11.3593	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral			x	x
E11.3599	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye			x	x
E11.37X1	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, right eye			x	x
E11.37X2	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, left eye			x	x
E11.37X3	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral			x	x
E11.37X9	Type 2 diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye			x	x
E13.311	Other specified diabetes mellitus with unspecified diabetic retinopathy with macular edema		x	x	x
E13.3211	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye		x	x	x
E13.3212	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye		x	x	x
E13.3213	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral		x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E13.3219	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E13.3291	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, right eye		x	x	x
E13.3292	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, left eye		x	x	x
E13.3293	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, bilateral		x	x	x
E13.3299	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy without macular edema, unspecified eye		x	x	x
E13.3311	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye		x	x	x
E13.3312	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye		x	x	x
E13.3313	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral		x	x	x
E13.3319	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E13.3391	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, right eye		x	x	x
E13.3392	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, left eye		x	x	x
E13.3393	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, bilateral		x	x	x
E13.3399	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy without macular edema, unspecified eye		x	x	x
E13.3411	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye		x	x	x
E13.3412	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye		x	x	x
E13.3413	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral		x	x	x
E13.3419	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E13.3491	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, right eye		x	x	x
E13.3492	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, left eye		x	x	x
E13.3493	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, bilateral		x	x	x
E13.3499	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy without macular edema, unspecified eye		x	x	x
E13.3511	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye		x	x	x
E13.3512	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye		x	x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E13.3513	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral		x	x	x
E13.3519	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, unspecified eye		x	x	x
E13.3521	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye		x	x	x
E13.3522	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye		x	x	x
E13.3523	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral		x	x	x
E13.3529	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, unspecified eye		x	x	x
E13.3531	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye		x	x	x
E13.3532	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye		x	x	x
E13.3533	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral		x	x	x
E13.3539	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, unspecified eye		x	x	x
E13.3541	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye		x	x	x
E13.3542	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye		x	x	x
E13.3543	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral		x	x	x
E13.3549	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, unspecified eye		x	x	x
E13.3551	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, right eye		x	x	x
E13.3552	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, left eye		x	x	x
E13.3553	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, bilateral		x	x	x
E13.3559	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, unspecified eye		x	x	x
E13.3591	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye			x	x
E13.3592	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye			x	x
E13.3593	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral			x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
E13.3599	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, unspecified eye			x	x
E13.37X1	Other specified diabetes mellitus with diabetic macular edema, resolved following treatment, right eye			x	x
E13.37X2	Other specified diabetes mellitus with diabetic macular edema, resolved following treatment, left eye			x	x
E13.37X3	Other specified diabetes mellitus with diabetic macular edema, resolved following treatment, bilateral			x	x
E13.37X9	Other specified diabetes mellitus with diabetic macular edema, resolved following treatment, unspecified eye			x	x
H32	Chorioretinal disorders in diseases classified elsewhere			x	x
H34.8110	Central retinal vein occlusion, right eye, with macular edema	x		x	x
H34.8111	Central retinal vein occlusion, right eye, with retinal neovascularization	x		x	x
H34.8112	Central retinal vein occlusion, right eye, stable	x		x	x
H34.8120	Central retinal vein occlusion, left eye, with macular edema	x		x	x
H34.8121	Central retinal vein occlusion, left eye, with retinal neovascularization	x		x	x
H34.8122	Central retinal vein occlusion, left eye, stable	x		x	x
H34.8130	Central retinal vein occlusion, bilateral, with macular edema	x		x	x
H34.8131	Central retinal vein occlusion, bilateral, with retinal neovascularization	x		x	x
H34.8132	Central retinal vein occlusion, bilateral, stable	x		x	x
H34.8190	Central retinal vein occlusion, unspecified eye, with macular edema	x		x	x
H34.8191	Central retinal vein occlusion, unspecified eye, with retinal neovascularization	x		x	x
H34.8192	Central retinal vein occlusion, unspecified eye, stable	x		x	x
H34.821	Venous engorgement, right eye	x		x	x
H34.822	Venous engorgement, left eye	x		x	x
H34.823	Venous engorgement, bilateral	x		x	x
H34.829	Venous engorgement, unspecified eye	x		x	x
H34.8310	Tributary (branch) retinal vein occlusion, right eye, with macular edema	x		x	x
H34.8311	Tributary (branch) retinal vein occlusion, right eye, with retinal neovascularization	x		x	x
H34.8312	Tributary (branch) retinal vein occlusion, right eye, stable	x		x	x
H34.8320	Tributary (branch) retinal vein occlusion, left eye, with macular edema	x		x	x
H34.8321	Tributary (branch) retinal vein occlusion, left eye, with retinal neovascularization	x		x	x
H34.8322	Tributary (branch) retinal vein occlusion, left eye, stable	x		x	x
H34.8330	Tributary (branch) retinal vein occlusion, bilateral, with macular edema	x		x	x
H34.8331	Tributary (branch) retinal vein occlusion, bilateral, with retinal neovascularization	x		x	x
H34.8332	Tributary (branch) retinal vein occlusion, bilateral, stable	x		x	x
H34.8390	Tributary (branch) retinal vein occlusion, unspecified eye, with macular edema	x		x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
H34.8391	Tributary (branch) retinal vein occlusion, unspecified eye, with retinal neovascularization	x		x	x
H34.8392	Tributary (branch) retinal vein occlusion, unspecified eye, stable	x		x	x
H35.051	Retinal neovascularization, unspecified, right eye			x	x
H35.052	Retinal neovascularization, unspecified, left eye			x	x
H35.053	Retinal neovascularization, unspecified, bilateral			x	x
H35.059	Retinal neovascularization, unspecified, unspecified eye			x	x
H35.3210	Exudative age-related macular degeneration, right eye, stage unspecified	x	x	x	x
H35.3211	Exudative age-related macular degeneration, right eye, with active choroidal neovascularization	x	x	x	x
H35.3212	Exudative age-related macular degeneration, right eye, with inactive choroidal neovascularization	x	x	x	x
H35.3213	Exudative age-related macular degeneration, right eye, with inactive scar	x	x	x	x
H35.3220	Exudative age-related macular degeneration, left eye, stage unspecified	x	x	x	x
H35.3221	Exudative age-related macular degeneration, left eye, with active choroidal neovascularization	x	x	x	x
H35.3222	Exudative age-related macular degeneration, left eye, with inactive choroidal neovascularization	x	x	x	x
H35.3223	Exudative age-related macular degeneration, left eye, with inactive scar	x	x	x	x
H35.3230	Exudative age-related macular degeneration, bilateral, stage unspecified	x	x	x	x
H35.3231	Exudative age-related macular degeneration, bilateral, with active choroidal neovascularization	x	x	x	x
H35.3232	Exudative age-related macular degeneration, bilateral, with inactive choroidal neovascularization	x	x	x	x
H35.3233	Exudative age-related macular degeneration, bilateral, with inactive scar	x	x	x	x
H35.3290	Exudative age-related macular degeneration, unspecified eye, stage unspecified	x	x	x	x
H35.3291	Exudative age-related macular degeneration, unspecified eye, with active choroidal neovascularization	x	x	x	x
H35.3292	Exudative age-related macular degeneration, unspecified eye, with inactive choroidal neovascularization	x	x	x	x
H35.3293	Exudative age-related macular degeneration, unspecified eye, with inactive scar	x	x	x	x
H35.33	Angioid streaks of macula	x	x	x	x
H35.81	Retinal edema	x		x	x
H40.89	Other specified glaucoma			x	x
H44.20	Degenerative myopia, unspecified eye			x	x
H44.21	Degenerative myopia, right eye			x	x
H44.22	Degenerative myopia, left eye			x	x
H44.23	Degenerative myopia, bilateral			x	x
H44.2A1	Degenerative myopia with choroidal neovascularization, right eye			x	x
H44.2A2	Degenerative myopia with choroidal neovascularization, left eye			x	x

ICD-10 Diagnosis Code	Description	Applies to HCPCS Code			
		J0178	J2503	J2778	J9035
H44.2A3	Degenerative myopia with choroidal neovascularization, bilateral eye			x	x
H44.2A9	Degenerative myopia with choroidal neovascularization, unspecified eye			x	x
H44.2B1	Degenerative myopia with macular hole, right eye			x	x
H44.2B2	Degenerative myopia with macular hole, left eye			x	x
H44.2B3	Degenerative myopia with macular hole, bilateral eye			x	x
H44.2B9	Degenerative myopia with macular hole, unspecified eye			x	x
H44.2C1	Degenerative myopia with retinal detachment, right eye			x	x
H44.2C2	Degenerative myopia with retinal detachment, left eye			x	x
H44.2C3	Degenerative myopia with retinal detachment, bilateral eye			x	x
H44.2C9	Degenerative myopia with retinal detachment, unspecified eye			x	x
H44.2D1	Degenerative myopia with foveoschisis, right eye			x	x
H44.2D2	Degenerative myopia with foveoschisis, left eye			x	x
H44.2D3	Degenerative myopia with foveoschisis, bilateral eye			x	x
H44.2D9	Degenerative myopia with foveoschisis, unspecified eye			x	x
H44.2E1	Degenerative myopia with other maculopathy, right eye			x	x
H44.2E2	Degenerative myopia with other maculopathy, left eye			x	x
H44.2E3	Degenerative myopia with other maculopathy, bilateral eye			x	x
H44.2E9	Degenerative myopia with other maculopathy, unspecified eye			x	x

BENEFIT CONSIDERATIONS

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy. Benefit coverage for an otherwise unproven service for the treatment of serious rare diseases may occur when certain conditions are met. See the Policy and Procedure addressing the treatment of serious rare diseases.

CLINICAL EVIDENCE

Proven

Neovascular Age-Related Macular Degeneration (AMD)

Aflibercept, pegaptanib, and ranibizumab are indicated for the treatment of neovascular age-related macular degeneration.[5-7]

Solomon et al evaluated the ocular and systemic effects of, and quality of life associated with, intravitreally injected anti-VEGF agents (pegaptanib, ranibizumab, and bevacizumab) for the treatment of neovascular AMD compared with no anti-VEGF treatment; and the relative effects of one anti-VEGF agent compared with another when administered in comparable dosages and regimens.[10] A database search identified 12 randomized controlled trials which included 5496 patients with neovascular AMD. Patients treated with any of the three anti-VEGF agents more often experienced improved vision, less often lost vision, and were less likely to be legally blind than patients treated with control interventions after one year of treatment. Additionally, these patients also showed improvements in structural areas of the eye that doctors use to monitor disease progression and treatment response compared with untreated patients. Compared with control treatments, treatment with ranibizumab or bevacizumab yielded larger improvements than pegaptanib. No trial compared pegaptanib directly with other anti-VEGF agents. When bevacizumab and ranibizumab were compared with each other, there were no major differences with respect to vision-related outcomes; there was, however, a large difference in cost between the two agents. Inflammation and increased pressure in the eye were the most common vision-related adverse events with anti-VEGF agents. Endophthalmitis was reported in < 1% of anti-VEGF-treated patients and no cases were reported in control groups. The occurrence of serious adverse health effects, such as high blood pressure and internal bleeding, was comparable across anti-VEGF-treated groups and control groups; however, the number of events was small relative to the number of people in the studies making it difficult to

detect any meaningful differences between groups. Few data were available for visual function (e.g., reading speed and critical print size), quality of life, and economic outcomes. The overall quality of the evidence was very good, with most trials having an overall low risk of bias. The results of the review indicated the effectiveness of anti-VEGF agents (pegaptanib, ranibizumab, and bevacizumab) in terms of maintaining visual acuity; ranibizumab and bevacizumab were also shown to improve visual acuity. The information available on the adverse effects of each medication do not suggest a higher incidence of potentially vision-threatening complications with intravitreal injection compared with control interventions; however, clinical trial sample sizes may not have been sufficient to detect rare safety outcomes.

In a multicenter, prospective, noninferiority, double-masked, randomized clinical trial, the relative efficacy and safety profile of bevacizumab versus ranibizumab intravitreal injections for the treatment of neovascular age-related macular degeneration (AMD) was evaluated.[62] Patients (n=501) aged ≥50 years were eligible if they presented with subfoveal neovascular AMD, with best-corrected visual acuity (BVCA) in the study eye of between 20/32 and 20/320 measured on the Early Treatment of Diabetic Retinopathy Study chart, and a lesion area of less than 12 optic disc areas (DA). Subjects were randomly assigned to intravitreal administration of bevacizumab (1.25 mg) or ranibizumab (0.50 mg), then followed for one year. A loading dose of three monthly intravitreal injections was administered to all subjects, followed by an as-needed regimen (one injection in case of active disease) for the remaining 9 months with monthly follow-up. The main outcome measure was the mean change in visual acuity at one year, with a noninferiority limit of five letters. In the per protocol analysis, bevacizumab was noninferior to ranibizumab (bevacizumab minus ranibizumab +1.89 letters; 95% confidence interval [CI], -1.16 to +4.93, p<0.0001). The intention-to-treat analysis was concordant. The mean number of injections was 6.8 in the bevacizumab group and 6.5 in the ranibizumab group (p=0.39). Both drugs reduced the central subfield macular thickness, with a mean decrease of 95 µm for bevacizumab and 107 µm for ranibizumab (p=0.27). There were no significant differences in the presence of subretinal or intraretinal fluid at final evaluation, dye leakage on angiogram, or change in choroidal neovascular area. The proportion of patients with serious adverse events was 12.6% in the bevacizumab group and 12.1% in the ranibizumab group (p=0.88). The proportion of patients with serious systemic or ocular adverse events was similar in both groups. Based on these results, bevacizumab was determined to be noninferior to ranibizumab for visual acuity at one year with similar safety profiles. Ranibizumab tended to have a better anatomic outcome.

A multi-center, single-blind, non-inferiority study was conducted by the CATT Research Group in 1,208 patients with neovascular age-related macular degeneration (AMD).[8] Participants were randomly assigned to receive intravitreal injections of either ranibizumab or bevacizumab on a monthly schedule or as needed with monthly evaluations. The primary outcome of the study was the mean change in visual acuity at one year, with a non-inferiority limit of 5 letters on the eye chart. The investigators reported that monthly administration of bevacizumab was equivalent to monthly administration of ranibizumab, with 8.0 and 8.5 letters gained, respectively. Results of as needed administration of the agents were determined to be equivalent, with bevacizumab recipients gaining 5.9 letters and ranibizumab recipients gaining 6.8 letters. Ranibizumab as needed was equivalent to monthly ranibizumab, while the comparison between bevacizumab as needed and monthly bevacizumab was inconclusive, The mean decrease in central retinal thickness was greater in the ranibizumab-monthly group (196 µm) than in the other groups (152 to 168 µm, p=0.03 by analysis of variance). Rates of death, myocardial infarction, and stroke were similar for patients receiving either treatment (p>0.20). However, the proportion of patients with serious systemic adverse events (primarily hospitalizations) was higher with bevacizumab than with ranibizumab (24.1% vs. 19.0%; risk ratio, 1.29; 95% confidence interval, 1.01 to 1.66), with excess events broadly distributed in disease categories not identified in previous studies as areas of concern. Therefore, the investigators recommended that differences in rates of serious adverse events should be further studied. At one year, bevacizumab and ranibizumab had equivalent effects on visual acuity when administered according to the same schedule. Ranibizumab given as needed with monthly evaluation had effects on vision that were equivalent to those of ranibizumab administered monthly.

Diabetic Macular Edema

Aflibercept and ranibizumab are indicated for the treatment of diabetic macular edema (DME).[5,7]

Virgili et al. evaluated the effects in preserving and improving vision and acceptability, including the safety, compliance with therapy and quality of life, of antiangiogenic therapy with anti-VEGF modalities for the treatment of diabetic macular oedema (DMO).[61] A database search was conducted which included randomized controlled trials (RCTs) comparing any antiangiogenic drugs with an anti-VEGF mechanism of action versus another treatment, sham treatment or no treatment in people with DMO. The primary outcome measured was the proportion of people improving or losing vision by three or more lines. Eighteen studies were included in this review. Approximately one in five people gained 3 lines of vision, using antiangiogenic therapy compared with laser, using seven to nine intraocular injections in the first year, and three or four injections in the second year. Benefits were also detected when the drug was compared to no treatment and when it was added to photocoagulation and compared to photocoagulation alone. Antiangiogenic treatment was well tolerated in these studies, with few reported injection-related adverse events and no increase in the number of reported overall and cardiovascular adverse events. Researchers concluded that the evidence utilized in the review was of high quality regarding efficacy compared to laser photocoagulation, the standard treatment, because the effects were large and consistent between studies. The evidence was also of moderate quality

regarding safety, since safety had to be confirmed in patients with higher morbidity, particularly regarding cardiovascular risk

Bevacizumab

Shoebi et al. reported the long-term results of intravitreal bevacizumab (IVB) injection alone or combined, at the time of first IVB injection, with intravitreal triamcinolone acetonide (IVT) for treatment of refractory diabetic macular edema (DME).[63] This randomized clinical trial enrolled 115 eyes of 101 patients with refractory DME and utilized three study arms: the IVB group (41 eyes) received three consecutive injections of 1.25 mg IVB at 6-week intervals; the IVB/IVT group (37 eyes) additionally received 2 mg of IVT at the time of first IVB injection; and the control (sham injection) group. Patients in the IVB and IVB/IVT groups were followed for a mean of 13.3 months and received retreatment with IVB alone whenever indicated. Main outcome measures were best corrected visual acuity (BCVA) and central macular thickness (CMT). The investigators found that at last follow up, CMT decreased significantly in the IVB group (p=0.013) but it was not significant (p=0.13) in the IVB/IVT group. Mean CMT improvement was 91 (95% CI, 20 to 161) microns and 57 (95% CI, -18 to 133) microns in the IVB and IVB/IVT groups, respectively. Mean BCVA improvement from baseline was 0.28 (95% CI, 0.18 to 0.38) logMAR (P=0.017) in the IVB group and 0.19 (95% CI, 0.08 to 0.30) logMAR (P=0.001) in the IVB/IVT group. There was no difference between the two groups in terms of visual improvment (p=0.42). In generalized linear mixed model, only the time interval between the last injection and CMT measurement was statistically significant (P=0.04). The same results were repeated for visual acuity (P=0.03). Based upon these findings, the authors concluded that three loading doses of IVB (added doses if required) have long-term beneficial effects for treatment of refractory DME and that adding triamcinolone to this regimen provides no additional long-term benefit.

Nepomuceno et al. compared visual acuity and spectraldomain optical coherence tomography (SDOCT) outcomes associated with intravitreal (IV) bevacizumab versus IV ranibizumab for the management of diabetic macular edema (DME) in a prospective, randomized trial.[64] Forty-eight patients (63 eyes) with center-involved DME were randomly assigned to receive 1.5 mg (0.06 cc) IV bevacizumab or 0.5 mg (0.05 cc) IV ranibizumab at baseline and monthly if central subfield thickness was greater than 275 µm. Forty-five patients (60 eyes) completed 48 weeks of follow-up. At baseline, mean ± standard error best-corrected visual acuity (BCVA) (logMAR) was 0.60 (20/80) ± 0.05 in the IV bevacizumab group and 0.63 (20/85) ± 0.05 in the IV ranibizumab group. A significant improvement in mean BCVA was observed in both groups at all study visits (P < 0.05); this improvement was significantly greater in the IV ranibizumab group compared with the IV bevacizumab group at weeks 8 (P = 0.032) and 32 (P = 0.042). A significant reduction in mean central subfield thickness was observed in both groups at all study visits compared with baseline (P < 0.05), with no significant difference in the magnitude of macular thickness reduction between groups. The mean number of injections was significantly higher (P = 0.005) in the IV bevacizumab group (9.84) than in the IV ranibizumab group (7.67). The investigators concluded that IV bevacizumab and IV ranibizumab are associated with similar effects on central subfield thickness in patients with DME through 1 year of follow-up. IV ranibizumab is associated with greater improvement in BCVA at some study visits, and the mean number of injections is higher in the IV bevacizumab group.

Pegaptanib

Sultan et al. conducted a randomized, multicenter, parallel-group trial to confirm safety and compare efficacy of intravitreal pegaptanib sodium versus placebo in subjects with diabetic macular edema (DME) involving the center of the macula associated with vision loss not due to ischemia.[12] During year one of the study, subjects received pegaptanib 0.3 mg or placebo every 6 weeks (total = 9 injections) and were eligible to receive focal/grid photocoagulation beginning at week 18. Subjects received injections as often as every 6 weeks per pre-specified criteria in the second year of the study. The primary efficacy endpoint was the proportion of subjects gaining ≥ 10 letters of visual acuity (VA) from baseline to year one. In total, 260 (pegaptanib, n=133; placebo, n=127) and 207 (pegaptanib, n=107; placebo, n=100) subjects were included in years 1 and 2 intent-to-treat analyses, respectively. A total of 49 of the 133 (36.8%) subjects from the pegaptanib group and 25 of the 127 (19.7%) from the placebo group experienced a VA improvement of ≥ 10 letters at week 54 compared with baseline (odds ratio [OR], 2.38; 95% confidence interval, 1.32-4.30; p=0.0047). In the pegaptanib-treated subjects, change in mean VA from baseline by visit was superior (p<0.05) to sham at weeks 6, 24, 30, 36, 42, 54, 78, 84, 90, 96, and 102. At week 102, pegaptanib-treated subjects gained, on average, 6.1 letters versus 1.3 letters for placebo (p<0.01). Fewer pegaptanib- than placebo-treated subjects received focal/grid laser treatment (week 54, 31/133 [23.3%] vs 53/127 [41.7%], respectively, p=0.002; week 102, 27/107 [25.2%] vs 45/100 [45.0%], respectively, p=0.003). The pegaptanib treatment group showed significantly better results on the National Eye Institute-Visual Functioning Questionnaire than sham for subscales important in this population. Pegaptanib was well tolerated; the frequencies of discontinuations, adverse events, treatment-related adverse events, and serious adverse events were comparable in the pegaptanib and placebo groups.

In a randomized, double-masked, multicenter, dose-ranging, controlled trial, Cunningham et al. evaluated the safety and efficacy of pegaptanib sodium injection in the treatment of diabetic macular edema (DME).[13] Study subjects (n=172) included those with a best-corrected visual acuity (VA) between 20/50 and 20/320 in the study eye, DME

involving the center of the macula, and for whom the investigator judged photocoagulation could be safely withheld for 16 weeks. The primary outcome measures were best-corrected VA, central retinal thickness at the center point of the central subfield as assessed by optical coherence tomography measurement, and the need for additional therapy with photocoagulation between weeks 12 and 36. Intravitreous pegaptanib 0.3 mg (n=44), pegaptanib 1 mg (n=44), pegaptanib 3 mg (n=42), or placebo (n=42) injections were administered upon study entry, at week 6, and at week 12 with additional injections and/or focal photocoagulation as needed for another 18 weeks. Final assessments were conducted at week 36. Median VA was better at week 36 with 0.3 mg (20/50), as compared with placebo (20/63) (p=0.04). A larger proportion of those receiving 0.3 mg gained VAs of ≥10 letters (approximately 2 lines) (34% vs. 10%, p=0.003) and ≥15 letters (18% vs. 7%, p=0.12). Mean central retinal thickness decreased by 68 microm with 0.3 mg, versus an increase of 4 microm with placebo (p=0.02). Larger proportions of those receiving 0.3 mg had an absolute decrease of both ≥100 microm (42% vs. 16%, p=0.02) and ≥75 microm (49% vs. 19%, p=0.008). Photocoagulation was deemed necessary in fewer subjects in each pegaptanib arm (0.3 mg vs. placebo, 25% vs. 48%; p=0.04). All pegaptanib doses were well tolerated. Endophthalmitis occurred in 1 of 652 injections (0.15% per injection; i.e., 1/130 [0.8%] pegaptanib subjects) and was not associated with severe visual loss. Overall, subjects assigned to pegaptanib had better VA outcomes, were more likely to show reduction in central retinal thickness, and were deemed less likely to need additional therapy with photocoagulation at follow-up.

Macular Edema Secondary to BRVO/CRVO

Afilbercept and ranibizumab are indicated for the treatment of macular edema following retinal vein occlusion (RVO).[5,7]

The efficacy and safety of intravitreal bevacizumab injections into eyes with macular edema secondary to central retinal vein occlusion (CRVO) was evaluated in a prospective clinical trial (n=45 eyes) by Zhang et al.[15] Study subjects were treated with 3 initial intravitreal bevacizumab injections of 1.25 mg at monthly intervals. Retreatment was based on central retinal thickness (CRT) measured by optical coherence tomography (OCT) performed monthly, while fluorescein angiography was performed every 3 months. Main outcome parameters were visual acuity (VA, using the Early Treatment of Diabetic Retinopathy Study protocol) and CRT in an 18-month follow-up period. Mean VA increased from 40.9 letters at baseline to 61.9 letters (+21 letters; p<0.001) at month 18; CRT decreased from 572.3 µm at baseline to 273.2 µm at month 18 (-299.1 µm; p<0.001). Neither age, duration of CRVO, baseline VA, nor baseline CRT was correlated with the change in VA. No drug-related systemic or ocular side effects were observed following intravitreal bevacizumab treatment.

The efficacy of intravitreal bevacizumab as the primary treatment of macular edema due to retinal vein occlusions was evaluated by Figueroa et al. in a study of patients diagnosed as having central retinal vein occlusion (CRVO) (n=18 eyes) or branch retinal vein occlusion (BRVO) (n=28 eyes) with visual acuity of less than 20/40 and macular edema (>300 microm central retinal thickness).[16] After an initial intravitreal injection of bevacizumab, re-treatment was performed if intraretinal or subretinal fluid with distortion of the foveal depression was found in optical coherence tomography. During a 6-month period, the mean number of injections per patient was 3.7 (BRVO group) and 4.6 (CRVO group). In the BRVO group, mean baseline logMAR visual acuity was 0.80 (SD 0.38) and macular thickness was 486.9 microm (SD 138.5 microm). After 6 months, mean logMAR visual acuity improved significantly to 0.44 (SD 0.34), p<0.001. Mean macular thickness decreased significantly to 268.2 microm (SD 62.5 microm), p<0.001. In the CRVO group, mean baseline logMAR visual acuity was 1.13 (SD 0.21) and macular thickness was 536.4 microm (SD 107.1 microm). Mean final logMAR visual acuity improved significantly to 0.83 (SD 0.45), p<0.001. Mean macular thickness decreased significantly to 326.17 microm (SD 96.70 microm), p<0.001. The investigators concluded that intravitreal bevacizumab is an effective primary treatment option for macular edema due to retinal occlusions. However, multiple injections are necessary to maintain visual and anatomic improvements.

Proliferative Diabetic Retinopathy

Aflibercept and ranibizumab are indicated for diabetic retinopathy [(Non Proliferative Diabetic Retinopathy (NPDR), Proliferative Diabetic Retinopathy (PDR)] in patients with diabetic macular edema (DME).[5,7]

Intravitreal bevacizumab has been studied as an adjunct to laser photocoagulation, to facilitate pars plana vitrectomy, and as a monotherapy for treatment of proliferating diabetic retinopathy (PDR).[17,59-60]

Ahmadieh et al. evaluated the effect of preoperative intravitreal bevacizumab (IVB) injections on the rate of early (≤4 weeks) postvitrectomy hemorrhage in patients (n=68) with proliferative diabetic retinopathy.[18] Subjects were randomly assigned to receive either 1.25 mg IVB (n=35) one week prior to surgery or control (n=33). The primary outcome measure was the incidence of early postvitrectomy hemorrhage. Secondary outcome measures included changes in best-corrected visual acuity (BCVA) and IVB-related adverse events. In the intention-to-treat analysis, the incidence of postvitrectomy hemorrhage 1 week and 1 month after surgery was significantly lower in the IVB group compared with the control group (p=0.023 and p=0.001, respectively). Mean BCVA improved from 1.88 logarithm of minimum angle of resolution (logMAR) units in both study groups before surgery to 0.91 logMAR units and 1.46 logMAR units 1 month after vitrectomy in the IVB and control groups, respectively (p=0.001). Resolution of

vitreous hemorrhage was observed in 9 eyes (25.7%) after IVB injection, obviating the need for vitrectomy; the corresponding figure was 2 eyes (6.1%) in the control group (p=0.028). The per-protocol analysis included 16 eyes in the IVB group and 18 eyes in the control group; postvitrectomy hemorrhage occurred less frequently 1 week and 1 month after surgery in the IVB group compared with the control group (p=0.033 and p=0.003, respectively). Mean improvement in BCVA 1 month after vitrectomy was -1.05 logMAR units in the IVB group and -0.42 logMAR units in the control group (p=0.004). No IVB-related complication was observed in the treatment group. The investigators concluded that IVB one week before vitrectomy appears to reduce the incidence of early postvitrectomy hemorrhage in diabetic patients. The need for vitrectomy may be decreased significantly in these cases as well.

In order to evaluate the safety and effectiveness of intravitreal bevacizumab (IVB) as an adjunct to vitrectomy, di Lauro et al. performed a randomized controlled trial on 72 eyes of 68 patients affected by vitreous hemorrhage (VH) and tractional retinal detachment (TRD) which occurred as a consequence of active proliferative diabetic retinopathy (PDR).[19] Participants were assigned in a 1:1:1 ratio to receive a placebo injection or an intravitreal injection of 1.25 mg of bevacizumab, either 7 or 20 days before the vitrectomy. Complete ophthalmic examinations and color fundus photography were performed at baseline and 1, 6, 12, and 24 weeks after the surgery. In the placebo group, intraoperative bleeding occurred in 19 cases (79.1%), the use of endodiathermy was necessary in 13 patients (54.1%), relaxing retinotomy was performed on one patient (4.1%), and in four cases (16.6%) iatrogenic retinal breaks occurred. The surgical mean time was 84 minutes (SD 12 minutes). In subjects receiving IVB seven days prior to vitrectomy, intraoperative bleeding occurred in two cases (8.3%) and the use of endodiathermy was necessary in two patients (8.3%). No iatrogenic breaks occurred during the surgery. The surgical mean time was 65 minutes (SD 18 minutes). For those subjects receiving IVB twenty days before vitrectomy, intraoperative bleeding occurred in three cases (12.5%), the use of endodiathermy was necessary in three patients (1.5%), and an iatrogenic break occurred in one patient (4.1%) while the delamination of fibrovascular tissue was being performed. The surgical mean time was 69 minutes (SD 21 minutes). The average difference in the surgical time was statistically significant between the placebo group and the 7-day IVB group (p=0.025), and between the placebo group and the 20-day IVB group (p=0.031). At completion of surgery, the retina was completely attached in all eyes. The researchers concluded that best surgical results are achieved performing the IVB 7 days preoperatively.

Neovascular Glaucoma

Ghosh et al. present the outcome of concomitant treatment with diode laser cyclophotocoagulation (CPC) and intravitreal bevacizumab (IVB) in painful eyes with poor visual potential in a case series of consecutively diagnosed neovascular glaucoma (NVG).[20] Twelve patients (14 eyes) were treated with CPC and concurrent IVB 0.05 mL (1.25 mg). Study end-points were lowering of intraocular pressure (IOP), regression of anterior segment neovascularization, and resolution of pain. The mean preoperative IOP was 42.1 ± 11.4 and was lowered to 16.6 ± 7.1 mmHg at 1-month post-CPC. Anterior segment neovascularization regressed dramatically within 1 week of IVB in 12 eyes. Thirteen eyes reported persistent relief of ocular pain at 6 months following treatment. The authors concluded that combined IVB and CPC treatment for NVG provides rapid control of anterior segment neovascularization and may lead to improved symptomatic relief and IOP control.

To evaluate the effect of intravitreal bevacizumab injection in cases of neovascular glaucoma, Ghanem et al. studied 16 eyes of 16 patients with rubeosis iridis and secondary glaucoma.[21] Patients were administered an intravitreal injection of bevacizumab (2.5 mg) and were followed for 2 months. Partial or complete regression of iris neovascularization was noted 1 week after injection of bevacizumab. Reproliferation of new vessels was detected in 25% of the cases after 2 months. The mean intraocular pressure (IOP) before injection was 28 ± 9.3 mm Hg under topical β-blocker and systemic acetazolamide. One week after injection, the IOP decreased to 21.7 ± 11.5 mm Hg (5 cases without anti-glaucoma drugs, 6 cases with topical β-blocker and 5 cases with both topical β-blocker and systemic acetazolamide). The authors concluded that intravitreal bevacizumab injection leads to regression of iris neovascularization with subsequent drop of IOP in eyes with neovascular glaucoma.

Moraczewski et al. report a retrospective, non-comparative, consecutive, interventional case series of the treatment of neovascular glaucoma with intravitreal bevacizumab in 56 eyes at the University of Miami, Florida, Bascom Palmer Eye Institute.[22] The authors' impression both clinically and from a review of available literature is that early diagnosis and treatment of NVG with intravitreal bevacizumab may lead to improved outcomes. If bevacizumab is administered when the anterior chamber angle is open at the time of NVG diagnosis, it is postulated that IOP may be controlled without the need for surgical procedures. This study underscores the concept that, if followed long enough, the majority of patients regardless of initial angle status and initial IOP lowering, will require surgical intervention for the control of IOP. The cumulative proportion of eyes requiring a second injection of bevacizumab increases linearly with time and is related to recurrent or persistent iris neovascularization or angle neovascularization. Bevacizumab induced regression of neovascularization is often temporary and recurrence is possible, while panretinal photocoagulation provides a more permanent reduction of the ischemic angiogenic stimulus. At this institution, treatment of NVG with intravitreal bevacizumab is the standard of care, including: 1) Administering intravitreal bevacizumab at the time of diagnosis of NVG; 2) Administering panretinal photocoagulation shortly thereafter, and; 3) lowering IOP medically and via placement of a drainage device if necessary.

Choroidal Neovascularization

Choroidal Neovascularization Secondary to Pathologic Myopia

Cha DM et al compared the long-term efficacy of versus bevacizumab for myopic choroidal neovascularization (CNV) in retrospective, multicenter, comparative, non-randomized study in 64 consecutive patients [ranibizumab (n=22) or bevacizumab (n=42 patients)].[9] Best-corrected visual acuity (BCVA) and central foveal thickness (CFT) on optical coherence tomography were evaluated before and after treatment. All the patients were followed for at least 12 months. BCVA (logarithm of the minimal angle of resolution) improved from 0.63 ± 0.30 to 0.43 ± 0.27, 0.41 ± 0.37, 0.40 ± 0.39, 0.39 ± 0.43, and 0.39 ± 0.42 at 1, 2, 3, 6, and 12 months after treatment in the ranibizumab group, and from 0.67 ± 0.28 to 0.52 ± 0.31, 0.49 ± 0.31, 0.47 ± 0.31, 0.42 ± 0.32, and 0.46 ± 0.43 in the bevacizumab group (all P < 0.05 compared with baseline BCVA in each group). CFT decreased by 20.21%, 19.58%, and 22.43% from the baseline 304 ± 76 μm at 3, 6, and 12 months after treatment in the former group, and by 15.20%, 15.67%, and 15.56% from the baseline 297 ± 62 μm in the latter group (all P < 0.05 compared with baseline CFT in each group). BCVA improvement and CFT reduction did not statistically differ when compared at the same periods from treatment between 2 groups. Neither ocular nor systemic safety problems appeared during follow up. Researchers concluded that the outcomes of the study showed a similar functional and anatomical improvement after treatment for ranibizumab and bevacizumab in patients with myopic CNV over a 12-month follow-up period.

In a phase III, 12-month, randomized, double-masked, multicenter, active-controlled study, researchers evaluated the efficacy and safety of ranibizumab 0.5 mg, guided by visual acuity (VA) stabilization or disease activity criteria, versus verteporfin photodynamic therapy (vPDT) in patients (n=277) with visual impairment due to myopic choroidal neovascularization (CNV).[11] Patients were randomized to receive ranibizumab on day 1, month 1, and thereafter as needed guided by VA stabilization criteria (group I, n = 106); ranibizumab on day 1 and thereafter as needed guided by disease activity criteria (group II, n=116); or vPDT on day 1 and disease activity treated with ranibizumab or vPDT at investigators' discretion from month 3 (group III, n = 55). Primary outcomes measured included average best-corrected visual acuity (BCVA) change from baseline to month 1 through months 3 (primary) and 6, mean BCVA change and safety over 12 months. Ranibizumab treatment in groups I and II was superior to vPDT based on mean average BCVA change from baseline to month 1 through month 3 (group I: +10.5, group II: +10.6 vs. group III: +2.2 Early Treatment Diabetic Retinopathy Study [ETDRS] letters; both P<0.0001). Ranibizumab treatment guided by disease activity was noninferior to VA stabilization-guided retreatment based on mean average BCVA change from baseline to month 1 through month 6 (group II: +11.7 vs. group I: +11.9 ETDRS letters; P<0.00001). Mean BCVA change from baseline to month 12 was +13.8 (group I), +14.4 (group II), and +9.3 ETDRS letters (group III). At month 12, 63.8% to 65.7% of patients showed resolution of myopic CNV leakage. Patients received a median of 4.0 (group I) and 2.0 (groups II and III) ranibizumab injections over 12 months. No deaths or cases of endophthalmitis and myocardial infarction occurred. CONCLUSIONS: Ranibizumab treatment, irrespective of retreatment criteria, provided superior BCVA gains versus vPDT up to month 3. Ranibizumab treatment guided by disease activity criteria was noninferior to VA stabilization criteria up to month 6. Over 12 months, individualized ranibizumab treatment was effective in improving and sustaining BCVA and was generally well tolerated in patients with myopic CNV.

Yoon et al. compared visual outcomes after treatment with intravitreal antivascular endothelial growth factor (anti-VEGF) injection or photodynamic therapy (PDT) in patients with myopic choroidal (CNV).[23] One hundred and forty-two eyes of 128 consecutive patients treated with anti-VEGF (ranibizumab or bevacizumab) and/or PDT for myopic choroidal neovascularization were retrospectively reviewed. Patients were categorized into 3 groups: PDT (51 eyes), anti-VEGF (63 eyes), and a combination group (PDT with anti-VEGF) (28 eyes). Corrected visual acuity values at baseline and 3, 6, 9, and 12 months after treatment were compared. The anti-VEGF group showed significant postoperative improvement in visual acuity compared with the PDT and combination groups (p=0.01 and 0.04, respectively). The anti-VEGF group demonstrated visual improvement from baseline at every follow-up visit after treatment (p=0.04, 0.02, 0.01, and 0.002, respectively). The anti-VEGF group showed visual improvement (Snellen equivalent) from 0.57 logarithm of the minimum angle of resolution (0.27) to 0.33 logarithm of the minimum angle of resolution (0.47) (p=0.01). Furthermore, 98.4% of patients in the anti-VEGF group and 92.8% of those in the combination group lost <15 letters from baseline visual acuity compared with 72.6% in the PDT group (p=0.001 and 0.02, respectively). In the anti-VEGF group, 39.7% of patients improved from baseline by 15 or more letters compared with 17.7% in the PDT group (p=0.02) and 21.4% in the combination group (p=0.07). Based on these findings, the investigators concluded that intravitreal anti-VEGF injection is superior to PDT alone or a combination of PDT with anti-VEGF for treating myopic choroidal neovascularization.

Vadalà et al. assessed the efficacy and safety of ranibizumab in the treatment of choroidal neovascularisation (CNV) caused by pathologic myopia (PM) in a prospective, multicentre, interventional case series.[24] Forty eyes of 39 consecutive patients with PM and CNV were treated with 'on demand' intravitreal injection of ranibizumab 0.5 mg. Final best corrected visual acuity (BCVA) and its change from baseline were the main outcome measures. Median follow-up was 13.3 ± 2 (range 12-18) months. Fifteen eyes (37.5%) had previously been treated with photodynamic therapy (PDT). The mean baseline logarithm of the minimum angle of resolution (logMAR) BCVA was 0.68 ± 0.34 (Snellen equivalent 20/131) and 21 ± 16 letters. The final mean logMAR BCVA was 0.27 ± 0.2 (p=0.008) (20/42) and

40.5 ± 14 letters (p=0.01). Mean final VA improved in 82.5% of patients, in 60% by 3 or more lines (median number of lines gained 2.9). Age and previous PDT did not influence the results (p>0.05). The mean number of injections was 2.8 ± 1.2 (range 1-6). No ocular or systemic side effects were observed. Ranibizumab was an effective treatment for stabilizing and improving vision with a low number of injections in 92.5% of patients with myopic CNV in a long-term follow-up.

Choroidal Neovascularization Secondary to Angioid Streaks/Pseudoxanthoma Elasticum

Finger et al. investigated the long-term effectiveness of intravitreal bevacizumab for treating active choroidal neovascularizations in pseudoxanthoma elasticum (PXE).[25] Fourteen patients (16 eyes) received intravitreal bevacizumab (1.5 mg), were evaluated monthly, and received further treatments depending on disease activity. Examinations included best-corrected visual acuity, biomicroscopy, optical coherence tomography, fluorescein angiography and indocyanine green angiography, fundus autofluorescence, and digital fundus photography. Areas of atrophy of the retinal pigment epithelium and retinal fibrosis were quantified using semiautomated detection on fundus autofluorescence images. Mean age of the cohort was 55 ± 13 years, and mean best-corrected visual acuity at baseline was 20/80 (logarithm of the minimum angle of resolution, 0.56, SD, 0.51). At last follow-up, after an average of 6.5 ± 5.7 injections over 28 months, best-corrected visual acuity was 20/40 (logarithm of the minimum angle of resolution, 0.31, SD, 0.32; p=0.04). Central retinal thickness was reduced from 254 ± 45 µm to 214 ± 40 µm (p=0.035). The size of retinal pigment epithelial atrophy and retinal fibrosis measured on fundus autofluorescence images increased in both the treated eye and the fellow eye (p<0.05). Best-corrected visual acuity of patients with early disease compared with that of those with advanced disease improved significantly more over the treatment course (20/25 vs. 20/63; p=0.008). The authors reported that intravitreal bevacizumab therapy demonstrates long-term effectiveness by preserving function in advanced disease and improving function in early disease. Best results of treating active choroidal neovascularizations in PXE are achieved when treatment starts as early in the disease as possible.

El Matri et al. evaluated the efficacy and safety of intravitreal bevacizumab for the treatment of choroidal neovascularization associated with angioid streaks in a retrospective case series of eighteen eyes of 17 patients treated between October 2006 and May 2008.[26] Ophthalmic evaluation, including best corrected visual acuity (BCVA), slit lamp biomicroscopic examination, optical coherence tomography (OCT) and fluorescein angiography, was performed before and after treatment. Retreatment was allowed every 4–6 weeks in case of persistent symptoms or CNV activity on OCT. Main outcome measures were changes in BCVA and central retinal thickness on OCT. The mean number of injections was 4.8 at one year. Twelve eyes (66.6%) received five injections or more. The mean BCVA at baseline was 20/80 (range 20/400 to 20/32) and improved to 20/44 (range 20/160 to 20/20) at 1 year (p=0.014). The BCVA improved by three or more lines in eleven eyes (61.11%) and remained within two lines of baseline in seven eyes (38.8%). Mean central retinal thickness was 404.2 µm (range 160–602 µm) at baseline and decreased to 300.5 µm (range 150–523 µm) at 1 year (p=0.022). No ocular or systemic complications were noted. The 1-year outcomes suggest intravitreal bevacizumab to be a promising treatment for CNV associated with angioid streaks, resulting in both functional and anatomical improvements. Repeated injections are needed to maintain these results. Further long term studies are required to confirm these findings.

Mimoun et al. retrospectively analyzed the efficacy of intravitreal ranibizumab injections for the management of choroidal neovascularization (CNV) in patients with angioid streaks.[27] In a nonrandomized, double-center, retrospective, interventional case series, patients were treated with intravitreal ranibizumab injections (0.5 mg/0.05 mL). The primary end point was the percentage of eyes with stable or improved visual acuity at the end of follow-up. Secondary end points were the percentage of eyes with stable or decreased macular thickness on optical coherence tomography and the percentage of eyes with persistent leakage on fluorescein angiography at the last follow-up examination. Thirty-five eyes of 27 patients were treated with repeated intravitreal ranibizumab injections (mean, 5.7 injections; range, 2 to 14 injections) for a mean of 24.1 months (range, 6 to 37 months). At the end of follow-up, visual acuity was stabilized or improved in 30 (85.7%) of 35 eyes. Macular thickness had stabilized or decreased in 18 (51.5%) of 35 eyes. At the last follow-up examination, on fluorescein angiography, no further leakage was observed in 23 (65.7%) of 35 eyes.

Myung et al. reported long-term results of intravitreal antivascular endothelial growth factor therapy in the management of choroidal neovascularization in patients with angioid streaks associated with pseudoxanthoma elasticum.[28] Nine eyes of nine consecutive patients were managed with either bevacizumab 1.25 mg/0.05 mL or ranibizumab 0.5 mg/0.05 mL. The main outcome measures were visual acuity and greatest lesion height as measured by optical coherence tomography. During the mean follow-up period of 28.6 months, eyes received an average of 8.4 injections. At baseline, the mean visual acuity was 20/368 (median, 20/60) and improved to 20/281 (median, 20/40) at the last visit (p=0.14). Visual acuity either improved or stabilized in all 9 eyes (100%). Serial optical coherence tomography measurements showed a mean of 353 mum at baseline and decreased to 146 mum at the last visit (p= 0.005). No complications were noted. These long-term results support the use of intravitreal antivascular endothelial growth factor therapy for the management of choroidal neovascularization in patients with pseudoxanthoma elasticum.

Choroidal Neovascularization Secondary to Ocular Histoplasmosis Syndrome (OHS)

Cionni et al. conducted a retrospective, comparative case series of 150 eyes in 140 patients treated with intravitreal bevacizumab (IVB) for choroidal neovascularization (CNV) secondary to presumed ocular histoplasmosis syndrome (POHS).[29] Subjects received either IVB monotherapy (n=117 eyes) or combination IVB and verteporfin photodynamic therapy (IVB/PDT) (n=34 eyes). Visual acuity (VA) at 12 and 24 months was analyzed. Secondary outcome measures included the number of injections per year and treatment-free intervals. For all patients, the average pretreatment logarithm of minimum angle of resolution (logMAR) was 0.63 (Snellen equivalent 20/86) with a 12-month logMAR VA of 0.45 (Snellen equivalent 20/56) and a 24-month logMAR VA of 0.44 (Snellen equivalent 20/55). The mean follow-up was 21.1 months with an average of 4.24 IVB injections per year. There was no significant difference in initial VA, VA at 12 months, VA at 24 months, or number of eyes with a 3-line gain between the IVB monotherapy and IVB/PDT groups. Thirty-eight percent (39/104) of eyes gained 3 lines or more, and 81.2% (84/104) of subjects had maintained or improved their starting VA at 1 year. The proportion of subjects maintaining a 3-line gain in VA was relatively preserved at 2 years (29.8%, 17/57) and 3 years (30.3%, 10/32) follow-up. There was no increase in the proportion of subjects losing 3 lines or more over 3 years of follow-up. The authors concluded that there is no significant difference in VA outcomes between IVB monotherapy versus IVB/PDT combination therapy. The use of IVB alone or in combination with PDT results in significant visual stabilization in the majority of patients with CNV secondary to POHS.

Shadlu et al. conducted a retrospective chart review of 28 eyes of 28 patients who underwent intravitreal administration of bevacizumab for treatment of choroidal neovascularization secondary to OHS.[30] The mean follow-up period was 22.43 weeks with patients receiving an average of 1.8 intravitreal injections. The investigators found that the treatment was of benefit to improve or stabilize the visual acuity in a significant majority (24 eyes, 85.7%) of patients with neovascular complications of OHS.

In a retrospective chart review of 54 eyes, Nielsen et al. studied the effect of treatment with intravitreal anti-VEGF therapy for choroidal neovascularization in ocular histoplasmosis syndrome.[31] Either bevacizumab or ranibizumab were administered on an average of 4.5 injections per patient per year of follow-up. Mean visual acuity improved from 20/53 to 20/26 over an average of 26.8 months. Vision loss was seen in only three eyes with loss limited to a single line of vision. Patients experienced no serious complications from treatment. Long-term intravitreal anti-VEGF therapy with bevacizumab or ranibizumab is beneficial in treatment of choroidal neovascularization in ocular histoplasmosis syndrome.

There are additional small published studies and reports that provide support for the use of both bevacizumab and ranibizumab to treat choroidal neovascularization secondary to pathologic myopia, angioid streaks/pseudoxanthoma elasticum, or ocular histoplasmosis syndrome (OHS).[32-46]

Professional Societies

Royal College of Ophthalmologists

The Royal College of Ophthalmologists released a scientific statement on bevacizumab use in medical ophthalmology in December 2011.[52] A working group of the Scientific Committee of the College considered the published literature relating to the efficacy and safety of bevacizumab (Avastin) and ranibizumab (Lucentis) in the treatment of the neovascular form of age-related macular degeneration (AMD). The College view is that the current published literature is consistent with the conclusion that bevacizumab and ranibizumab are equally effective in the treatment of neovascular age-related macular degeneration and there is no convincing evidence of a clinically significant difference in the incidence of serious adverse events between the two groups. Since then, the College has made a revised statement stating there is clear evidence that, despite the lack of a licence, bevacizumab is a safe and effective drug for the treatment of neovascular AMD.

American Society of Retina Specialists (ASRS)

According to the American Society of Retina Specialists (ASRS), bevacizumab is being used by a large number of retinal specialists who believe that it is reasonable and medically necessary for the treatment of some patients with macular edema and abnormal retinal and iris neo-vascularization.[53]

American Academy of Ophthalmology (AAO)

The American Academy of Ophthalmology (AAO) supports the use of intravitreal injection therapy using anti-vascular endothelial growth factor (VEGF) agents (e.g., aflibercept, bevacizumab and ranibizumab) is the most effective way to manage neovascular AMD and represents the first line of treatment.[54]

In their Diabetic Retinopathy Preferred Practice Pattern, the AAO states that intravitreal injections of anti-vascular endothelial growth factor (VEGF) agents have been shown to be an effective treatment for center-involving diabetic macular edema and also as an alternative therapy for proliferative diabetic retinopathy.[55]

In their Retinal Vein Occlusions Preferred Practice Pattern, the AAO states that Macular edema may complicate both CRVOs and BRVOs. The safest treatment for the associated macular edema is the use of antivascular endothelial growth factors (anti-VEGFs). Intravitreal corticosteroids, with the associated risk of glaucoma and cataract formation, have demonstrated efficacy. Also, laser photocoagulation in BRVO has a potential role in treatment.[65]

In 2014 the AAO released a clinical statement entitled 'Verifying the Source of Compounded Bevacizumab for Intravitreal Injections – 2014.[56] Their recommendations are as follows:

- To reduce the risk of infection to patients, the following steps are recommended when sourcing bevacizumab (Avastin) for intravitreal injections:
  - Select a compounding pharmacy accredited by the PCAB, which adheres to quality standards for aseptic compounding of sterile medications (USP <797>). *Please note: PCAB does not track or keep record of specific medications that a pharmacy can compound.*
  - Record the lot numbers of the medication in the patient's record and in a logbook or spreadsheet in case the numbers are needed for tracking later.

In addition, Ophthalmic Mutual Insurance Company's (OMIC) Risk Management Recommendations for Preparations of Avastin specify:

- Using proper aseptic technique during the preparation and administration of the injection.
- "Credentialing" the compounding pharmacy where you send the prescription for intravitreal bevacizumab (Avastin) by:
  - Verifying that the compounding pharmacy is licensed/registered in the state it is dispensing.
  - Inquiring how the pharmacy compounds bevacizumab (Avastin). (The pharmacy should state that it complies with USP <797>.)
  - Asking the pharmacy if it is an accredited compounding pharmacy.
- Requesting that the compounding pharmacy prepare the medication for ophthalmic use, confirms the dose and sterility, identifies a syringe suitable for the protein, provides storage and "beyond-use" instructions, and indicates the vial lot number.

The informed consent process with the patient should include a discussion of the risks and benefits of treatment and treatment alternatives where the off-label status of bevacizumab (Avastin) for neovascular AMD should be included in the discussion.

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Medicare does not have a National Coverage Determination (NCD) for the use of vascular endothelial growth factor (VEGF) inhibitors; such as Avastin® (bevacizumab), Eylea™ (aflibercept), Lucentis® (ranibizumab) and Macugen® (pegaptanib). Local Coverage Determinations (LCDs) exist; see the LCDs for Drugs and Biologics (Non-chemotherapy) and Vascular Endothelial Growth Factor Inhibitors for the Treatment of Ophthalmological Diseases.

Medicare covers outpatient (Part B) drugs that are furnished "incident to" a physician's service provided that the drugs are not usually self-administered by the patients who take them. See the Medicare Benefit Policy Manual, Chapter 15, §50 - Drugs and Biologicals. (Accessed June 7, 2018)

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POLICY HISTORY/REVISION INFORMATION

Date	Action/Description
03/01/2019	Reorganized policy template; simplified and relocated *Instructions for Use* and *Benefit Considerations* section. Reformatted list of applicable ICD-10 diagnosis codes and added columns identifying the applicable drug product. Archived previous policy version 2018D0042K.
09/01/2018	Annual review of the policy. Removed retinopathy of prematurity from unproved section in coverage rationale. Updated CMS statement and references. Approved by the National Pharmacy & Therapeutics Committee on 08/17/2018. Policy 2018D0042J archived.
01/01/2018	Off cycle review. Removed diabetic macular edema requirement for diabetic retinopathy for Lucentis. Approved by the National Pharmacy & Therapeutics Committee on 11/17/2017. Policy 2017D0042I archived.
10/01/2017	Annual review of the policy. No change to the coverage rationale. Updated CMS statement and References. Approved by the National Pharmacy & Therapeutics Committee on 08/18/2017. Policy 2014D0042H archived.
10/01/2016	Coding update. Removed ICD-9 codes. Removed ICD-10 codes: E08.321, E08.331, E08.341, E08.351, E08.351, E08.359, E09.321, E09.331, E09.341, E09.351, E09.359, E10.321, E10.331, E10.341, E10.351, E10.359, E11.321, E11.331, E11.341, E11.351, E11.359, E13.321, E13.331, E13.341, E13.351, E13.359, H34.811, H34.812, H34.813, H34.819, H34.831, H34.832, H34.833, H34.839, H35.32. Added ICD-10 codes: E08.3211, E08.3212, E08.3213, E08.3219, E08.3291, E08.3292, E08.3293, E08.3299, E08.3311, E08.3312, E08.3313, E08.3319, E08.3391, E08.3392, E08.3393, E08.3399, E08.3411, E08.3412, E08.3413, E08.3419, E08.3491, E08.3492, E08.3493, E08.3499, E08.3511, E08.3512, E08.3513, E08.3519, E08.3521, E08.3522, E08.3523, E08.3529, E08.3531, E08.3532, E08.3533, E08.3539, E08.3541, E08.3542, E08.3543, E08.3549, E08.3551, E08.3552, E08.3553, E08.3559, E08.3591, E08.3592, E08.3593, E08.3599, E08.37X1, E08.37X2, E08.37X3, E08.37X9, E09.3211, E09.3212,

Date	Action/Description
	E09.3213, E09.3219, E09.3291, E09.3292, E09.3293, E09.3299, E09.3311, E09.3312, E09.3313, E09.3319, E09.3391, E09.3392, E09.3393, E09.3399, E09.3411, E09.3412, E09.3413, E09.3419, E09.3491, E09.3492, E09.3493, E09.3499, E09.3511, E09.3512, E09.3513, E09.3519, E09.3521, E09.3522, E09.3523, E09.3529, E09.3531, E09.3532, E09.3533, E09.3539, E09.3541, E09.3542, E09.3543, E09.3549, E09.3551, E09.3552, E09.3553, E09.3559, E09.3591, E09.3592, E09.3593, E09.3599, E09.37X1, E09.37X2, E09.37X3, E09.37X9, E10.3211, E10.3212, E10.3213, E10.3219, E10.3291, E10.3292, E10.3293, E10.3299, E10.3311, E10.3312, E10.3313, E10.3319, E10.3391, E10.3392, E10.3393, E10.3399, E10.3411, E10.3412, E10.3413, E10.3419, E10.3491, E10.3492, E10.3493, E10.3499, E10.3511, E10.3512, E10.3513, E10.3519, E10.3521, E10.3522, E10.3523, E10.3529, E10.3531, E10.3532, E10.3533, E10.3539, E10.3541, E10.3542, E10.3543, E10.3549, E10.3551, E10.3552, E10.3553, E10.3559, E10.3591, E10.3592, E10.3593, E10.3599, E10.37X1, E10.37X2, E10.37X3, E10.37X9, E11.3211, E11.3212, E11.3213, E11.3219, E11.3291, E11.3292, E11.3293, E11.3299, E11.3311, E11.3312, E11.3313, E11.3319, E11.3391, E11.3392, E11.3393, E11.3399, E11.3411, E11.3412, E11.3413, E11.3419, E11.3491, E11.3492, E11.3493, E11.3499, E11.3511, E11.3512, E11.3513, E11.3519, E11.3521, E11.3522, E11.3523, E11.3529, E11.3531, E11.3532, E11.3533, E11.3539, E11.3541, E11.3542, E11.3543, E11.3549, E11.3551, E11.3552, E11.3553, E11.3559, E11.3591, E11.3592, E11.3593, E11.3599, E11.37X1, E11.37X2, E11.37X3, E11.37X9, E13.3211, E13.3212, E13.3213, E13.3219, E13.3291, E13.3292, E13.3293, E13.3299, E13.3311, E13.3312, E13.3313, E13.3319, E13.3391, E13.3392, E13.3393, E13.3399, E13.3411, E13.3412, E13.3413, E13.3419, E13.3491, E13.3492, E13.3493, E13.3499, E13.3511, E13.3512, E13.3513, E13.3519, E13.3521, E13.3522, E13.3523, E13.3529, E13.3531, E13.3532, E13.3533, E13.3539, E13.3541, E13.3542, E13.3543, E13.3549, E13.3551, E13.3552, E13.3553, E13.3559, E13.3591, E13.3592, E13.3593, E13.3599, E13.37X1, E13.37X2, E13.37X3, E13.37X9, H34.8110, H34.8111, H34.8112, H34.8120, H34.8121, H34.8122, H34.8130, H34.8131, H34.8132, H34.8190, H34.8191, H34.8192, H34.8310, H34.8311, H34.8312, H34.8320, H34.8321, H34.8322, H34.8330, H34.8331, H34.8332, H34.8390, H34.8391, H34.8392, H35.3210, H35.3211, H35.3212, H35.3213, H35.3220, H35.3221, H35.3222, H35.3223, H35.3230, H35.3231, H35.3232, H35.3233, H35.3290, H35.3291, H35.3292, H35.3293. Policy 2016D0042G archived.
08/01/2016	Annual review of the policy. No change to the coverage rationale. Modified drug policy contents to conform to new policy template with no changes to clinical intent. Updated CMS statement, Clinical Evidence, and References. Approved by the National Pharmacy & Therapeutics Committee on 06/22/2016. Policy 2014D0042F archived.
10/1/2015	Updated Applicable Codes for ICD-10 transition. Policy 2015D0042E archived.
7/1/2015	Off-cycle review. Added diabetic retinopathy in patients with diabetic macular edema (DME) as a proven use to Eylea and Lucentis. Updated CMS, Benefits Consideration, Clinical Evidence, U.S. FDA and References. Approved by the National Pharmacy & Therapeutics Committee on 04/14/2015. Policy 2014D0042D archived.
12/1/2014	Annual review of policy. Added DME as a proven use of Eylea. Updated clinical evidence and references. Updated list of ICD-9 codes (added 115.02, 115.12, 115.92, 360.21, and 363.43) and associated ICD-10 codes. Approved by the National Pharmacy & Therapeutics Committee on 10/14/2014. Policy 2014D0042C archived.
2/1/2014	Annual review of policy. Clinical evidence and references updated. Approved by the National Pharmacy & Therapeutics Committee on 11/12/2013. Policy 2013D0042B archived.
1/1/2013	Full policy review. Policy revised. Added macular edema secondary to BRVO/CRVO to the proven uses for aflibercept. Updated FDA section for both aflibercept and ranibizumab. Added J0178 which becomes effective 1/1/2013 and replaces Q2046. Clinical evidence and references updated. Approved by the National Pharmacy & Therapeutics Committee on 11/13/2012. Policy 2012D0042A archived.
11/14/2012	New policy 2012D0042A. Approved by the National Pharmacy & Therapeutics Committee on 04/10/2012. Avastin (bevacizumab) policy 2012D0024O retired.

INSTRUCTIONS FOR USE

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard benefit plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. UnitedHealthcare Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.