Clinical Policy: Verteporfin (Visudyne)

Reference Number: CP.PHAR.187
Effective Date: 03.01.16
Last Review Date: 05.21
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Verteporfin (Visudyne®) is a light activated drug used in photodynamic therapy.

FDA Approved Indication(s)

Visudyne is indicated for the treatment of patients with predominantly classic subfoveal choroidal neovascularization (CNV) due to:

- Age-related macular degeneration (AMD)
- Pathologic myopia
- Presumed ocular histoplasmosis

Limitation(s) of use: There is insufficient evidence to indicate Visudyne for the treatment of predominantly occult subfoveal CNV.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Visudyne is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Choroidal Neovascularization (must meet all)**:**

1. Diagnosis of subfoveal CNV due to one of the following (a, b, or c):
   a. AMD;
   b. Pathologic myopia;
   c. Presumed ocular histoplasmosis;
2. Prescribed by or in consultation with an ophthalmologist;
3. Age ≥ 18 years;
4. For AMD, member meets one of the following (a or b):
   a. Failure of bevacizumab intravitreal solution, unless contraindicated or clinically significant adverse effects are experienced;
      **Prior authorization may be required for bevacizumab intravitreal solution. Requests for IV formulations of Avastin, Mvasi, and Zirabev will not be approved*
   b. Disease has progressed after use of a vascular endothelial growth factor (VEGF) as first-line treatment;

5. For CNV due to pathologic myopia, failure of intravitreal Avastin or Lucentis®, unless clinically significant adverse effects are experienced or both are contraindicated;
   **Prior authorization may be required for Avastin and Lucentis*
6. Dose does not exceed 6 mg/m^2 body surface area.

Approval duration:
HIM/Medicaid – 3 months (1 dose)
Commercial – Length of Benefit

B. Central Serous Chorioretinopathy (off-label) (must meet all)**:**
1. Diagnosis of central serous chorioretinopathy confirmed by retinal scan;
2. Prescribed by or in consultation with an ophthalmologist;
3. Disease is characterized as chronic or recurrent as evidenced by one of the following (a or b):
   a. Persistent subretinal fluid for ≥ 3 months;
   b. Persistent subretinal fluid for < 3 months and prescriber attestation that member is symptomatic (e.g., blurry central vision);
4. Member meets one of the following (a or b):
   a. Member is not taking medications from any of the following classes: corticosteroids, stimulants, decongestants, or erectile dysfunction medications;
   b. Documentation that prescriber has evaluated medications as risk factors if they are from any of the following classes: corticosteroids, stimulants, decongestants, or erectile dysfunction medications;
5. Dose does not exceed 6 mg/m^2 body surface area.

Approval duration:
HIM/Medicaid – 3 months (1 dose)
Commercial – Length of Benefit

C. Other diagnoses/indications
1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Choroidal Neovascularization (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by one of the following (a, b, c, or d):
   a. Detained neovascularization;
   b. Improvement in visual acuity;
   c. Maintenance of corrected visual acuity from prior treatment;
   d. Supportive findings from optical coherence tomography or fluorescein angiography;

3. Recent fluorescein angiography, conducted at least 3 months after the last treatment, shows recurrent or persistent choroidal neovascular leakage;
4. If request is for a dose increase, new dose does not exceed 6 mg/m^2 body surface area.

Approval duration:
HIM/Medicaid – 3 months (1 dose)
Commercial – Length of Benefit

B. Central Serous Chorioretinopathy (off-label):
1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AMD: age-related macular degeneration
CNV: choroidal neovascularization
mCNV: myopic choroidal neovascularization
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
bevacizumab (Avastin®)	**Neovascular (wet) AMD:** 1.25 to 2.5 mg administered by intravitreal injection every 4 weeks	2.5 mg/month
	mCNV: 0.05 mL initial intravitreal injection, followed by monthly evaluation for additional injections as needed	0.5 mL/month

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Beovu® (brolucizumab)	**Neovascular (wet) AMD:** 6 mg (1 via) administered by intravitreal injection every 4 weeks for the first 3 months, then every 8 or 12 weeks thereafter	6 mg (1 vial) every 2 months after loading period
Eylea® (aflibercept)	**Neovascular (wet) AMD:** 2 mg (0.05 mL) administered by intravitreal injection once a month for 3 months then 2mg every 2 months.	2 mg/month
Lucentis® (ranibizumab)	**Neovascular (wet) AMD:** 0.5 mg (0.05 mL) administered by intravitreal injection once a month. <u>Alternative dosing:</u> Once monthly injections for three months followed by 4-5 doses dispersed among the following 9 months Or Treatment may be reduced to one injection every 3 months after the first four injections if monthly injections are not feasible.	0.5 mg/month
	Myopic CNV: 0.5 mg (0.05 mL) administered by intravitreal injection once a month for up to 3 months. Patients may be retreated if needed.	0.5 mg/month
Macugen® (pegaptanib)	**Neovascular (wet) AMD:** 0.3 mg (0.09 mL) administered by intravitreal injection every 6 weeks	0.3 mg/6 weeks

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Porphyria
  - Hypersensitivity
- Boxed warning(s): none reported

Appendix D: General Information

- In the ANti-VEGF Antibody for the Treatment of Predominantly Classic CHORoidal Neovascularisation in AMD (ANCHOR) trial, the number of patients that lost fewer than 15 letters at 12 months was achieved by 96.4% of patients treated with Lucentis 0.5 mg compared to 64.3% of patients treated with Visudyne ($p < 0.001$). Rate of intraocular

inflammation was higher for patients treated with Lucentis 0.5 mg at 15% compared to Visudyne at 2.8%.

- In the RADIANCE, a Phase III, 12-month, multicenter, randomized, double-masked, active-controlled trial, Lucentis was compared to vPDT (Visudyne and photodynamic therapy) for the treatment of mCNV. Lucentis 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 $p < 0.0001$). Lucentis 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Predominantly classic subfoveal CNV due to AMD, pathologic myopia or presumed ocular histoplasmosis	6 mg/m^2 IV diluted with 5% dextrose to a final volume of 30 mL infused over 10 minutes	6 mg/m^2 IV

VI. Product Availability

Vial for reconstitution: 15 mg (2 mg/mL after reconstitution)

VII. References

1. Visudyne Prescribing Information. Bridgewater, NJ: Valeant Ophthalmics; February 2017. Available at: www.visudyne.com. Accessed September 17, 2020.
2. American Academy of Ophthalmology Retina/Vitreous Panel. Preferred Practice Pattern® Guidelines. Age-Related Macular Degeneration. San Francisco, CA: American Academy of Ophthalmology; October 2019. Available at: www.aao.org/ppp. Accessed September 17, 2020.
3. Diaz RI, Sigler EJ, Rafieetary MR, Calzada JI. Ocular histoplasmosis syndrome. *Surv Ophthalm*. 2015; 60(4): 279-295.
4. Wolf S, Valciuniene VJ, Laganovska G, et al. RADIANCE: a randomized controlled study of ranibizumab in patients with choroidal neovascularization secondary to pathologic myopia. *Ophthalmology*. 2014; 121(3):682-92.e2. doi: 10.1016/j.ophtha.2013.10.023. Epub 2013 Dec 8.
5. Salehi M, Wenick S, Law HA, Evans JR, Gehlbach P. Interventions for central serous chorioretinopathy: a network meta-analysis. *Cochrane Database Syst Rev.* 2016; 12. doi: 10.1002/14651858.CD011841.pub2.
6. Hanumunthadu D, Tan ACS, Singh SR, et al. Management of chronic central serous chorioretinopathy. *Indian J Ophthalmol*. 2018; 66(12): 1704-1714.

7. Van Rijssen TJ, van Dijk EHC, Yzer S, et al. Central serous chorioretinopathy: towards an evidence-based treatment guideline. *Progress in Retinal and Eye Research.* 2019; 73. doi: 10.1016/j.preteyeres.2019.07.003.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3396	Injection, verteporfin, 0.1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Medicaid: Removed age restriction. Removed restriction that lesion must be ≤ 5400 microns in greatest linear diameter for predominantly classic CNV. Added definition for occult CNV. Added option for contraindication/clinically significant adverse effects to anti-VEGF trial requirement. Removed max dose criterion, and instead incorporated dosing as a quantity limit (1 dose per 3 month approval period). Removed safety criteria. For continuation: Modified "Currently receiving…" to "Previously received…" to account for as needed dosing. Added requirement for documentation of positive response to therapy. Specified that FA should be at least 3 months after the last treatment.	03.17	03.17
1Q18 annual review: Policy combined for Medicaid and commercial lines of business; For Medicaid: Added specialist requirement, Removed fluorescein angiography for diagnosis due to addition of specialist, Added age limit, Expanded VEGF requirement for AMD and pathologic myopia specifically to bevacizumab or other VEGF inhibitors, Added redirection to Lucentis for mCNV due to clinical superiority, Removed allowed indication for occult CNV per limitation of use; References reviewed and updated.	11.23.17	02.18
1Q 2019 annual review: no significant changes; references reviewed and updated.	11.20.18	02.19
1Q 2020 annual review: no significant changes; added Avastin biosimilar to therapeutic alternatives; references reviewed and updated.	10.23.19	02.20
Ad Hoc update: clarified redirection from bevacizumab to Avastin as compounding pharmacies often break standard Avastin vials into smaller dosages specifically for ophthalmic use and there is a temporary CPT code not currently available to biosimilars.	10.01.20	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2021 annual review: no significant changes; added HIM line of business; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	12.01.20	02.21
Ad Hoc update: updated redirection to "bevacizumab intravitreal solution" given availability of generic bevacizumab intravitreal solution and considering goal was to minimize use of IV bevacizumab products, most notably biosimilars; converted redirection language to "must use"	03.04.21	
Ad Hoc update: added off-label criteria for central serous chorioretinopathy per health plan request.	03.23.21	05.21
Ad Hoc update: converted redirection language from "must use" to "Failure of" bevacizumab intravitreal solution.	08.03.21	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.